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Archives of Dermatology and Syphilology

VOLUME 30 SEPTEMBER 1934 NUMBER 3

DERMATOPHYTES

NATURAL GROUPING BASED ON THE FORM OF THE SPORES AND ACCESSORY ORGANS

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NEW YORK

There is a well recognized need in medical mycology for a more logical and usable classification of the dermatophytes. A better knowledge of the morphology of these fungi is necessary before one can expect to improve on the present systems. The classification of fungi is based on the manner in which the spores are borne and on their characters. By studying the type of spores developing after a so-called sexual process one is better able to determine probable relationships between species and genera. Many fungi belonging to the form class fungi imperfecti have no known sexual reproduction. The classification of these fungi depends on the vegetative spores or conidia which do not always indicate real relationships. As has often been pointed out, it may therefore happen that a given genus of the fungi imperfecti includes species of diverse origins. Nevertheless, a critical study of the characters of the spores, of their development, and of the sterigmata which bear them often indicates fundamental differences between groups within such a form genus which would be missed by a more casual study.

In classifying species of the ringworm fungi, which are fungi imperfecti, one must depend on a study of vegetative structures and conidia. One is dependent on these as well in placing the dermatophytes in a general classification since the reports of asci in cultures of Trichophyton are not well substantiated. The ringworm fungi reproduce by two types of spores which have usually been called aleuries and fuseaux, but which should be called conidia and macroconidia because they are in all essential respects like those spore forms in other fungi. Besides the spores some of the dermatophytes bear other structures which have been used to differentiate species and to suggest generic relationships. Certain species form closely coiled hyphae or spirals of characteristic form; some produce "organes nodulaires" which resemble the ascogonia of the ascomycetes; some show peculiarities in hyphal cells or in the terminal branches of the vegetative mycelium. A patient

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search for these structures, the use of different culture mediums and studies of variations have indicated that some of these structures are not so specific as was once believed. A spiral hypha, for example, which has been considered typical of certain varieties of Trichophyton mentagrophytes [1] (Trichophyton gypseum) may, under the proper conditions, appear in other species or genera. Furthermore, the essential similarity between the conidia of such diverse forms as T. mentagrophytes and Trichophyton Schoenleini (Achorion Schoenleini) implies a closer relationship between these forms than is indicated by their present positions in different genera. The present confusion in the classification and nomenclature of the dermatophytes has come about because these facts have been ignored.

The new species and genera proposed in some recent classifications are not satisfactory because they are based on characters which either are not constantly present or are of a quantitative nature and as such are not convenient for the differentiation of species. In some cases this has resulted in the wide separation of closely related forms. This is true of the classifications proposed by Ota and Langeron,[2] Vuillemin,[3] Grigorakis [4] and Guiart and Grigorakis.[5] The following instance illustrates this point. Ota and Langeron [2] have discarded the genus Microsporum and have placed in their new genus, Sabouraudites, all the species of Microsporum and Trichophyton in which they find macroconidia (fuseaux). This did not result in a natural division and was later modified. The mere fact that two species of dermatophytes have macroconidia does not mean that they necessarily belong in the same genus. There are natural lines of separation in the dermatophytes, and

1. Throughout this article several unfamiliar names of species appear. The law of priority requires that these be substituted for those which have been applied at a later date but have become familiar through use. It is inconvenient to make these changes, but it is fortunate that in most cases there is a well authenticated earlier name to which one can turn. It is the more necessary to make these changes since many of the familiar names of species appear to be synonyms. Ota and Kawatsuré (Sur l'inoculabilité à l'animal du Trichophyton interdigitale Priestley, Ann. de parasitol. **11**:206, 1933; Sur le Sabouraudites ruber et ses variétés, ibid. **11**:476, 1933) have called attention to much of this synonymy, and it will be referred to again in this article. The first use of mentagrophytes as a specific name is that of C. Robin (Histoire naturelle des végétaux parasites, Paris, J.-B. Baillière, 1853, p. 40).

2. Ota, M., and Langeron, M.: Nouvelle classification des dermatophytes, Ann. de parasitol. **1**:305, 1923.

3. Vuillemin, P.: Classification normale, classement auxiliaire et groupement pratique des champignons, Compt. rend. Acad. d. sc. **180**:102, 1925.

4. Grigorakis, L.: (*a*) Contribution à l'étude des dermatomycoses, Compt. rend. Acad. d. sc. **179**:1423, 1924; (*b*) Recherches sur les dermatophytes, Ann. d. sc. nat. **7**:165, 1925; (*c*) Dermatophytes et dermatomycoses, Ann. de dermat. et syph. **10**:18, 1929.

5. Guiart, J., and Grigorakis, L.: La classification botanique des champignons des teignes, Lyon méd. **141**:369, 1928.

these depend on the macroconidia. They depend, however, not on the mere presence or absence, but on the type, of macroconidia. The old genus Microsporum embraces a natural group in which the macroconidia are large, thick-walled and spindle-shaped. In contrast, the genus Trichophyton includes species in which there are macroconidia which are clavate and comparatively thin-walled. These are generically distinct from the species of Microsporum with which Ota and Langeron's classification would place them. The other classifications mentioned are even more confusing. The species of Trichophyton, if such there be, which never produce macroconidia show their relationship to the genus by other morphologic features.

Langeron and Milochevitch [6] have to some extent simplified the classification by throwing into synonymy several names in what has been known as the T. gypseum group. Their treatment of genera, however, is unsatisfactory. Ota and Kawatsuré [7] have further broadened the concept of the species which includes the gypseum forms, and in a second contribution they have dealt with the synonymy of Trichophyton rubrum. These revisions have been based on morphologic studies of cultures grown on natural mediums, and on inoculations of animals. A study of the genesis and of the mature forms of spores indicates a need for a further revision in the same direction of simplification as that taken by these authors. As a basis, then, for a more usable classification of these forms this article offers a study of spores and spore production and of some of the other structures to be found in some common species.

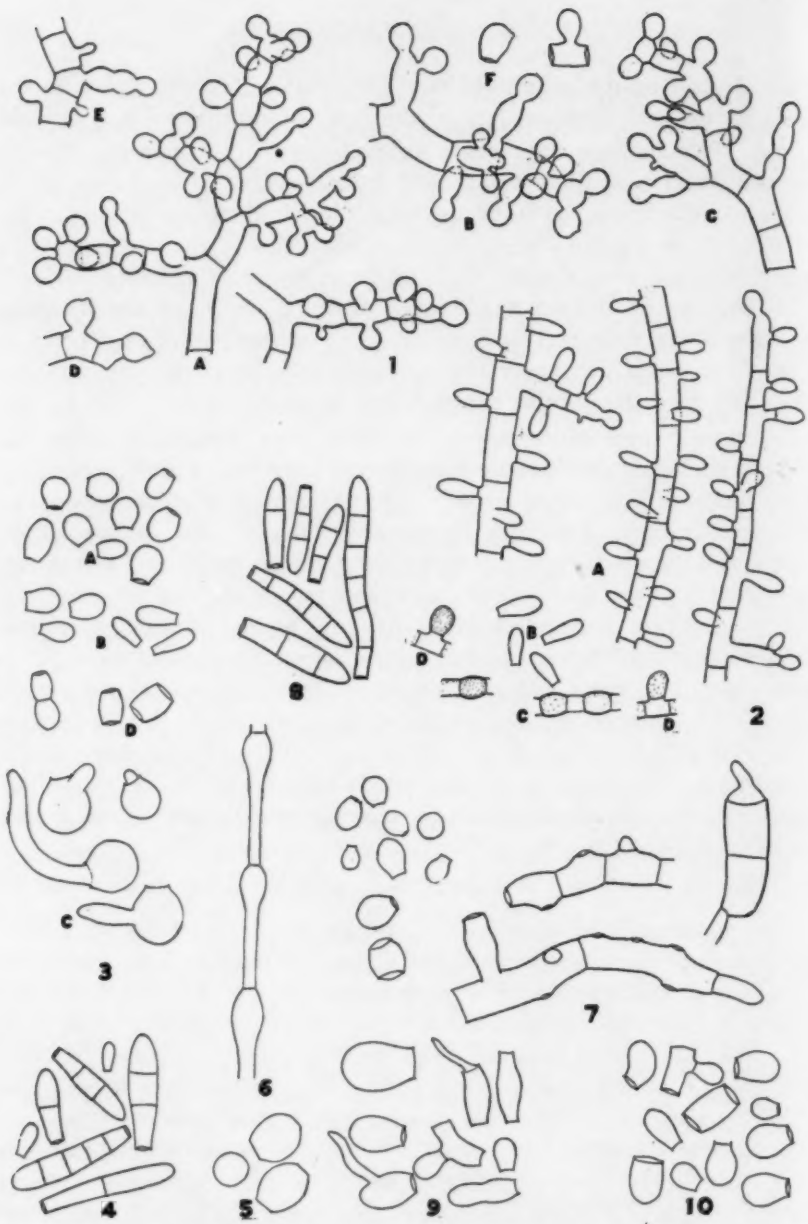
METHOD OF STUDY

It has been possible to follow carefully the development of conidiophores and spores by the use of a special culture cell. Henrici [8] described a certain type of slide culture in which agar is run under a cover slip fastened to a slide. Certain modifications in technic make this method a good one for supplementing studies of tube and plate cultures of the ringworm fungi. By using a thin shaving of cow's horn in place of the agar a somewhat better development of spores is obtained while vegetative growth is reduced. Suitable thin shavings of horn can be secured by scraping with a piece of glass. A shaving about 1 sq. cm. in area is sterilized and placed on a flamed slide and covered with a thin, flamed cover slip, and the latter is fastened in

6. Langeron, M., and Milochevitch, S.: Morphologie des dermatophytes sur milieux naturels et milieux à base de polysaccharides. Essai de classification, Ann. de parasitol. **8**:465, 1930.

7. Ota, M., and Kawatsuré, S.: Ann. de parasitol. **11**:206, 1933; Sur le Sabouraudites ruber et ses variétés, ibid. **11**:476, 1933.

8. Henrici, A.: Molds, Yeasts and Actinomycetes, New York, John Wiley and Sons, 1930, p. 33.



Figs. 1-10.—Reproductive structures of Trichophyton. *1*, conidiophores of T. mentagrophytes, showing modes of growth and development of conidia: *A*, *B* and *C*, branching conidiophores; *D*, *E* and *F*, origin of conidia; × 1,300. *2*, sporulation in T. mentagrophytes: *A*, Acladium type; *B*, conidia from "pleomorphic" cultures; *C*, chlamydospores; *D*, aleuries; × 1,300. *3*, conidia of T. mentagrophytes: *A*, characteristic types; *B*, from a "pleomorphic" culture; *C*, germination; *D*, subterminal conidia; × 1,300. *4*, macroconidia of T. mentagrophytes; × 500. *5*, chlamydospores of T. mentagrophytes; × 500. *6*, "racquet mycelium" in T. mentagrophytes; × 500. *7*, conidia of T. mentagrophytes and the scars on old cells from which conidia have fallen; × 1,300. *8*, macroconidia from a culture of T. exsiccatum; × 500. *9*, conidia of T. indicum; × 1,300. *10*, conidia of T. Sabouraudi; × 1,300.

place by running hot paraffin down on both sides. Sterile water is run in from the lower edge until it covers the horn (fig. 15). By means of a fine needle the horn shaving is inoculated from above with a few spores; the cell is sealed above and below with hot paraffin, and the preparation is incubated at room temperature. The slides may be kept on edge by thrusting one end into a coil spring.

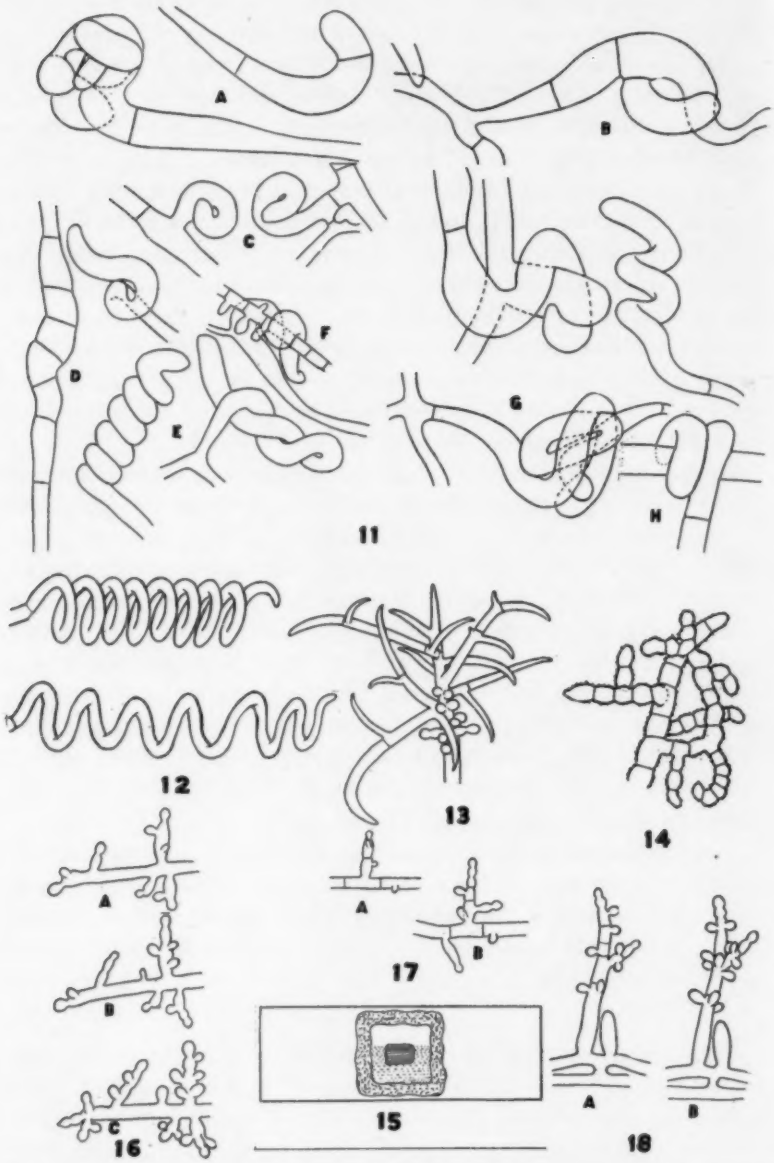
If all the operations are carried out carefully and quickly few cultures will be contaminated, and if several are made some will be thin enough and satisfactory in other respects for subsequent study. The advantages of such a culture cell are that in it individual conidiophores can be studied as they develop, and one can study it as often as desired without contaminating it since it is completely sealed. If the cell is properly made the high power objective can be used to examine its entire depth, and the oil immersion lens can be used to examine occasional conidiophores which are near the cover slip.

With a culture chamber such as the one described, individual conidiophores were studied at intervals over varying periods of time. The early stages of development can be found since the young conidiophore is usually differentiated from the vegetative branches by its dense protoplasm, its somewhat greater diameter and its manner of leaving the hypha at an angle of about 90 degrees (figs. 1 *E*, 16 and 17). Its subsequent development into a short, often branched spore-bearing structure can be watched. After it reaches a certain stage its growth usually ceases, probably because the oxygen is exhausted and staling products accumulate in the small culture cell. The intermediate stages of somewhat restricted branching and spore formation can, however, be followed as shown in figures 16, 17 and 18.

This method of study was used to supplement studies made from plate and tube cultures on a variety of mediums. In the latter the fungi grew more luxuriantly, and conidiophores were more fully developed (fig. 1), but it was impossible, of course, to study the development of a particular conidiophore.

CONIDIUM

The conidium ("aleurie" of French authors) of the dermatophytes varies in size and shape in different species. It may be almost spherical as in T. mentagrophytes (fig. 3 *A*); it may be long or clavate as in Microsporum felineum (fig. 20) and in "pleomorphic" forms of T. mentagrophytes (figs. 2 *B* and 3 *B*). In Trichophyton Sabouraudi (Trichophyton acuminatum) the same single spore culture contains conidia varying widely in size and shape (fig. 10). Regardless of the size or shape of conidia in these different types, all have certain important features in common. The base of the conidium of the dermatophytes is broad, and under high magnifications shows clearly in many species the collar by which it was attached to the hypha (fig. 3 *A*). Within this



Figs. 11-18.—Development of reproductive and other structures in T. mentagrophytes. *11,* ascogonia; × 1,300. *12,* spiral hyphae; × 1,300. *13,* antler-like hyphae associated with the development of conidial masses; × 500. *14,* later development of the antler-like hyphae; × 500. *15,* slide culture cell used in observing the development of individual conidiophores; × ½. *16,* stages in the development of a conidiophore: *B,* after five hours; *C,* after twenty-four hours; × 500. *17,* development of a conidiophore during a seventeen hour interval; × 500. *18,* development of a conidiophore during a sixteen hour interval; × 500.

collar the septum which forms the base of the conidium is thin, so that in a large mature spore it may bulge. Germination may occur at this point but does not necessarily do so. At germination the conidia become much swollen (fig. 3 *C*).

In all the dermatophytes the conidium is hyaline and thin-walled; its shape is from subspherical to clavate. Usually a given strain forms predominantly one general type as to shape. Wide variations in size and shape may, however, be found within the same single spore strain. The size and shape are also dependent on the condition of the culture and on the success with which any "pleomorphic" change has been prevented during the propagation of the strain. Since the conidia in a given strain are capable of these great variations that fact must be considered in setting the limits of any one species.

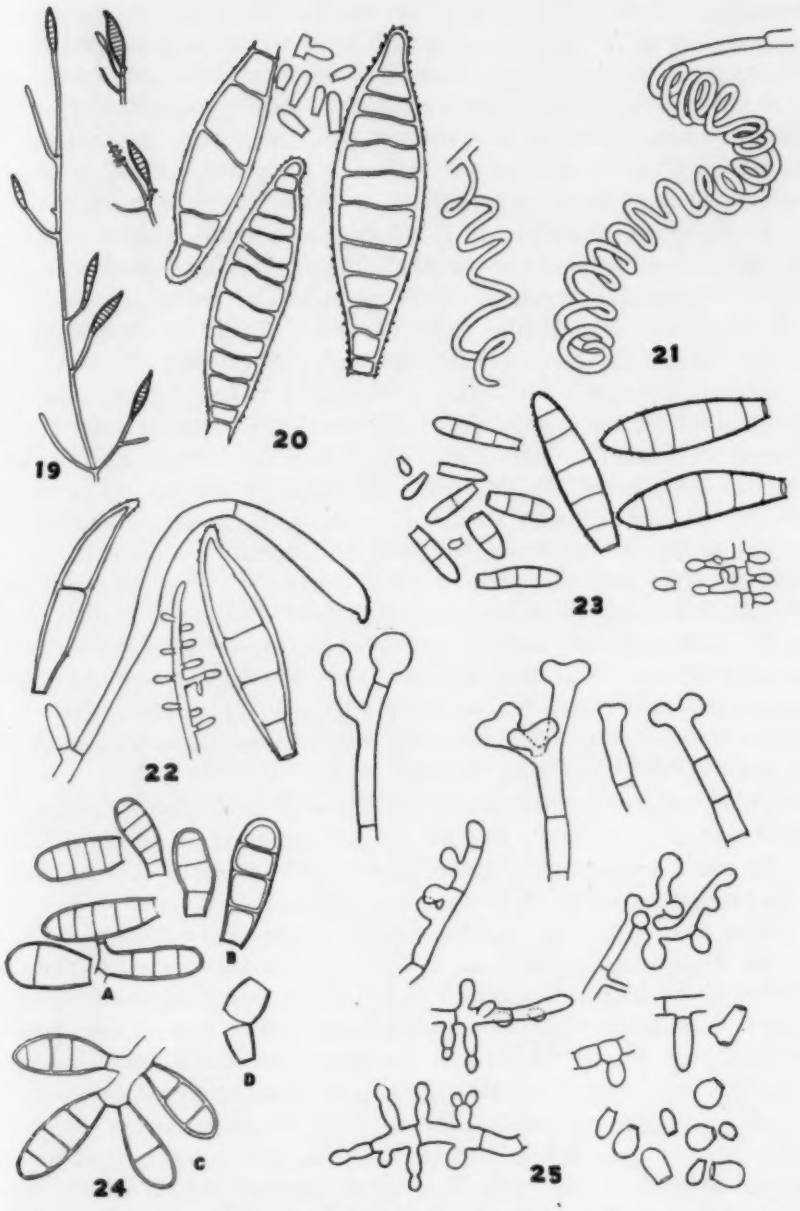
The production of conidia reaches its highest expression in the dermatophytes in T. mentagrophytes, in which the conidiophore may become highly specialized (fig. 1 *A, B* and *C*). The typical conidiophore in this species arises as a short side branch from a vegetative hypha (figs. 1*E* and 16*A*). As it elongates it may branch, and it and its branches may assume a beaded appearance due to the presence of more or less regular constrictions. Eventually septums form at all these constrictions, but the first septums appear toward the base. Many of the potential branches in these cultures, and presumably in plate and test tube cultures, reach the dimensions of spores and cease to grow (fig. 16). Others develop into longer branches which bear lateral and terminal spores, or, in the case of tube and plate cultures, may branch again (fig. 1 *A* and *C*). The young spore or the young branch appears first as a thin apiculate swelling on the side or tip of a fertile hypha or conidiophore (fig. 1 *D*). This increases in size until it is from subspherical to ovoid or clavate. At the same time the pore by which it is connected with the parent hypha increases in size so that at maturity the faceted base of the spore is comparatively large. This is then a case of spore development by budding, but it is quite different from the budding in yeasts in which the daughter cell is, in typical cases, pinched off at a point on the wall of the mother cell. It is similar to the type of spore formation found in Hormodendrum in which the young spores appear by budding at the end of a conidiophore or chain of spores. In contrast it is interesting to recall the radically different type of spore chain to be found in Penicillium and Aspergillus, in which the conidiophore is more highly specialized and retains the function of forming spores so that the youngest spore is always at the base of the chain. One may again, without implying any relationship, compare the conidial apparatus of Trichophyton with that of Hormodendrum. In both it is capable of continued centripetal growth; it is indeterminate in nature. Continued development seems to depend on conditions of

growth in that part of the culture and not on any inherent morphologic factor. A young bud arising on a conidiophore of Trichophyton may develop into a spore and terminate growth at that point, or it may bud again to become the subterminal element of a short chain of spores. Ota and Langeron [2] have called attention to these chains of spores.

So far as could be determined in this study the chain of spores does not usually exceed three or four cells in length, and of these, all except the terminal cells might on casual examination be pronounced cells of the conidiophore rather than spores. However, the subterminal cells, as this method of study shows, are sporelike in origin and function. When one mounts material from a mature tube or plate culture of T. mentagrophytes for examination innumerable small sporelike bodies float out in the mounting medium. Many of these can without hesitation be pronounced spores. Others which have been freed by the dissociation of the subterminal cells of the sporogenous complex are of the approximate size of the former, or slightly larger, but differ somewhat in shape (fig. 3*D*). They are usually truncated at both ends, although this condition may not always be apparent. Germination tests show that they function readily as spores. In other words, most of the cellular elements of the complex reproduction structure of T. mentagrophytes are sporelike in nature and merit the name of conidia.

A simpler type of sporulation is to be found in "pleomorphic" cultures and in such species as T. Sabouraudi in which chains of spores are not usually formed and the spores are borne laterally as sessile buds or on short stalks. In some strains of T. mentagrophytes the conidia may be much larger and more varied in size than in the more common strains just described (fig. 7). This is true also in T. Sabouraudi and related forms. These spores are in all other respects similar to those just described. These larger and varied spores are of the type found in T. Schoenleini when that species sporulates (fig. 23). Many strains of this species produce in culture only chlamydospores, abortive conidia and various abnormal structures. However, in some strains, besides these abortive organs, true conidia may be found. This observation seems helpful in the attempt to place these forms in a logical system of classification, and its application is considered later.

Often in some species (T. Sabouraudi) and occasionally in others (some strains of T. mentagrophytes) the protoplasm from a sporogenous cell passes almost completely into the spore or spores which it bears. Such a spore may remain fastened to its empty parent cell (fig. 2*D*) and is called in the terminology of Vuillemin an aleurie. It does not differ significantly from the more numerous spores of identical origin and shape which separate readily from the conidiophore and are clearly conidia. In some cases occasional cells of the conidiophore or of fertile hyphae assume the character of chlamydospores by a concentration of



Figs. 19-25.—Reproductive organs in species of Microsporum. *19*, macroconidia of M. felineum; × 110. *20*, conidia and macroconidia of M. felineum; × 500. *21*, spiral hyphae in an old maltose agar culture of M. felineum; × 500. *22*, conidia and macroconidia of M. Audouini; × 500. *23*, conidia and macroconidia of M. gypseum; × 500. *24*, macroconidia of E. floccosum; × 500. *25*, conidia of T. Schoenleini and some hyphal structures found in the abnormal mycelium of that species; × 1,300.

protoplasm while adjacent cells are exhausted by the production of spores (fig. 2*C*). Bodin [9] compared these spores with those formed in the genus Endoconidium. In Endoconidium, however, spores are pushed out successively from the hollow end of a specialized conidiophore. These spores of Trichophyton, on the contrary, are the result of a concentration, often at the expense of adjacent cells of the vegetative hyphae or of the conidiophores, and are true chlamydospores.

In pleomorphic cultures of T. mentagrophytes and in other dermatophytes the conidiophore may be simple or even lacking. In the simplest type of sporulation in these forms the spores are merely sessile budlike outgrowths from hyphal cells (fig. 2*A*). Bodin [9] studied this type of sporulation in Microsporum equinum and compared it with that occurring in the genus Acladium. This has often since been called the Acladium type of sporulation. Sabouraud [10] designated such fertile hyphae as "thyrses" to differentiate them from the more compact branching conidiophores where the spores are borne *en grappes*. The spores of the Acladium type are usually elongate, with smaller bases than the spores previously described (fig. 2*B*). Since they replace the more elaborate type of sporulation when a culture becomes "pleomorphic" they have been regarded as degenerate types. Despite their differences in size and shape they also bear the faceted base of the typical dermatophyte conidium. We know with certainty that the two types of spores are genetically related because they appear in the same single spore strain under different conditions and stages of development, as well as in normal cultures of many species.

Some of the dermatophytes, particularly Trichophyton violaceum, produce conidia so rarely that their classification on mycologic grounds alone may be uncertain. Spores appear, sometimes in abortive form, in some strains of T. violaceum, however, and there seem to be good reasons for considering the organism a species of Trichophyton.

In the genus Trichophyton conidia may be subspherical to clavate; they may be borne on more or less complex branching conidiophores or as sessile buds on undifferentiated hyphae; they may be shed readily or they may remain fastened to the parent cell at maturity, and they vary in size. Forms intermediate to the extreme types are common.

The elongate or clavate form of conidium is borne by species of Microsporum. In general the conidia of species of Microsporum are larger than those of Trichophyton, but they are clearly of the same general type of fungus spore (figs. 20, 22 and 23), as pointed out by Fox and Blaxall.[11] They may be sessile on the hyphae but are usually

9. Bodin, E.: Le Microsporum du cheval, Arch. de parasitol. **1**:379, 1898.

10. Sabouraud, R.: Les teignes, Paris, Masson & Cie, 1910.

11. Fox, T. C., and Blaxall, F. R.: An Inquiry into the Plurality of Fungi Causing Ringworm in Human Beings as Met with in London, Brit. J. Dermat. **8**:241, 291, 337 and 377, 1896.

pediculate. They may be borne in close association with the more highly specialized macroconidia (fig. 19) or on more remote parts of the mycelium. When conidia appear in T. Schoenleini they are, as stated, of the same type as those found in other species of Trichophyton. The conidia of species formerly placed in the genus Endodermophyton are usually larger, but are also of the same type (fig. 9). Conidial formation has not been observed in Epidermophyton floccosum (Epidermophyton inguinale).

A comparison of the dermatophyte conidia with the spores found in other fungi shows that similar spores are formed by some of the Gymnoasceae. Of the forms examined, Gymnoascus setosus Eidam, Myxotrichum uncinatum and Arachniotus aureus have conidia which are subspherical to pear-shaped and have broad bases surrounded by a collar such as is present in the conidia of Trichophyton. These differ from the conidia of dermatophytes in size, color or the manner in which they are borne, although they are sufficiently alike to suggest a relationship.

The conidium of the dermatophytes is, then, a characteristic structure, and while it shows some variety in size and shape the differences between conidia of different species and genera are much the same as those which are readily found in the conidia within such a species as T. mentagrophytes. Briefly, the conidia of the dermatophytes are one-celled, thin-walled, hyaline and subspherical or pear-shaped to clavate, with relatively broad faceted bases, 2 to 4 by 3 to 6 microns in size, and are borne as sessile buds on the sides of undifferentiated hyphae or on conidiophores which are simple or more or less elaborately branched.

MACROCONIDIA

Three types of macroconidia (the "fuseaux" of French authors) are found in the dermatophytes. Intermediate forms suggest that the three types have a common origin, but in their typical forms they are quite different and serve to set apart the three groups in which they are found. When young they may resemble each other, but as they mature they become differentiated.

The macroconidia of Trichophyton are clavate with blunt ends and with broad bases which are encircled by a collar marking the place of attachment to the conidiophore. The walls are thin and smooth, and there may be constrictions where the cross-septums appear. The macroconidia of Epidermophyton are usually clavate to egg-shaped. They are proportionately wider than those of Trichophyton, and the walls are thicker but smooth as in Trichophyton. The macroconidia of Microsporum are typically spindle-shaped with pointed tips, but they also have the broad, faceted and collared base which characterizes the conidia and macroconidia of the dermatophytes. In some species, for

example in Microsporum gypseum (fig. 23), the shape may be somewhat modified, but a comparison shows its affinities with the Microsporum type. The Microsporum macroconidia are large, with thick rough walls. Following the brief review of the distinguishing characters of the three types of macroconidia each type will be considered in more detail.

In Trichophyton the number of macroconidia to be found depends on the species, the strain and the conditions for growth. Some strains regularly produce numerous macroconidia while others form only a few or form them only occasionally in subcultures. In some species they may be lacking. In many cases, when none are to be found in the aerial mycelium they are fairly numerous in the thin layer left on the surface of the agar after the aerial mycelium is peeled back. In a strain which usually shows only a few, certain subcultures may, without apparent cause, suddenly develop them in great numbers (fig. 8).

The macroconidium of T. mentagrophytes is a clavate spore which may be as much as twice the diameter of the branch bearing it, and it may be of nearly uniform diameter, or somewhat inflated toward the distal end (fig. 4). It may have one or several septums. The walls are thin and hyaline. In some strains it is easy to find gradations between large, clavate conidia and small macroconidia (fig. 4). The macroconidia suggest differentiated chlamydospores somewhat more than the conidia. In an occasional strain they are hardly more than hyphal tips which are differentiated by becoming several-celled and are then detached bodily from the parent hypha. They vary greatly in size. Those which are one or two celled may be 4 by 15 microns while the larger ones may reach 6 by 50 microns in size.

A second type is formed in Epidermophyton floccosum (Epidermophyton cruris, Epidermophyton inguinale) in which the macroconidia reach a higher degree of development and constitute (besides the chlamydospores) the only known spore form for the species (fig. 24). In this species the macroconidia are from two to several celled, typically from oval to egg-shaped, with smooth, slightly thickened walls which sometimes show a yellow color. In some old spores the inner limits of the thick wall are difficult to see. As a result one gets the impression that the protoplast has shrunk away from the wall (fig. 24 *B*). They are borne occasionally in dense clusters suggesting bunches of bananas. In most strains they are more scattered. In some subcultures, particularly in those grown under unfavorable conditions, the typical macroconidia are replaced wholly or in part by chlamydospores. Many of these appear to be fragments of broken or abortive macroconidia (fig. 24). The Epidermophyton type of macroconidia is to be distinguished from the first by thickened walls, an ovoid or egglike shape and greater abundance.

In the species of Microsporum the macroconidia are of the third type and even more specialized. They are best developed in such a form as M. felineum, a species which infects animals (figs. 19 and 20). In this species the macroconidia are more abundant than the conidia, although the latter are also found and may predominate in old or pleomorphic cultures. The macroconidia of Microsporum, as contrasted with the clavate macroconidia of Trichophyton, are spindle-shaped and suggest the name of "fuseaux" used by the French medical mycologists. Those of M. felineum are long and have pointed ends and as many as fifteen cross-walls in mature spores (fig. 20). These cross-walls may appear wavy in optical section, and are often placed diagonally (fig. 20). The walls are thick, and the outer wall, particularly toward the ends, is often rough or tuberculate. These thick walls seem to be characteristic. They may present a stratified appearance, and in M. felineum, for example, they bear a strong superficial resemblance to the lignified walls of some higher plant cells.

Microsporum Audouini, a common cause of epidemics of ringworm of the scalp in children, reproduces in culture principally by clavate conidia, but it forms a few macroconidia, at least in most strains. These are smaller and have fewer cross-walls than those of M. felineum (fig. 22). The external walls are thinner than in the latter species; they may be smooth or roughened only at the ends; and in many spores the protoplast seems to be abnormally watery or vacuolate. All these observations suggest that M. Audouini may be a degenerate form of M. felineum. This possibility is further strengthened by the characters of occasional strains of M. Audouini, which when first isolated in culture produce abundant and well formed macroconidia tending toward the M. felineum type.

M. gypseum (Achorion gypseum) reproduces in culture principally by macroconidia, although conidia are also present. The macroconidia of this species are not so pointed as those of M. felineum, and have fewer cross-walls (fig. 23). The walls are thinner than in that species but thicker than those of Trichophyton and rough.

While at least three types of macroconidia are found in the genus Microsporum depending on the species, these are sufficiently like each other and sufficiently different from those of Trichophyton and Epidermophyton to characterize a genus and constitute the third type of macroconidia of the dermatophytes. They differ from the first two types in their spindle shape, large size, numerous septums and thick, usually rough walls.

There are, then, three natural groups of the dermatophytes, and these are to be differentiated, in part by the types of conidia (in Trichophyton and Microsporum), but principally by the types of macroconidia. There appear to be ample grounds for this generalization,

but it is admitted that however natural the grouping, the deficiencies of certain dermatophytes mar its perfection from the standpoint of practical use. For example, T. violaceum rarely forms conidia in either synthetic or natural mediums; typical macroconidia may not be found in many strains of Trichophyton, and only with difficulty in many strains of M. Audouini. However, one familiar with these forms recognizes them by other characters, and these can be used in the preparation of a key.

The macroconidia of the dermatophytes are to be differentiated from those of Alternaria with which they have sometimes been confused (Neto and Martins [12]). The muriform spores of Alternaria are divided by both cross and longitudinal walls. The macroconidia of the dermatophytes have only cross-walls.

The cells into which the macroconidium is divided are each multinucleate in contrast with the single-celled conidium which is usually uninucleate (Grigorakis,[4b] Emmons [13]). The macroconidia are of the same rank as the small conidia. When single conidia and single macroconidia are planted they give rise to identical colonies, except that the colony from a macroconidium usually develops more rapidly. This is presumably because of the larger amount of protoplasm and stored food in the larger spore. When the conidium germinates it usually sends out one germination tube, sometimes from the base, but usually from the side or top (fig. 3 *C*). When a macroconidium germinates it usually sends out one or more germination tubes from each cell, and the young colony thus receives a more vigorous start. However, subcultures from such single conidium and single macroconidium cultures are identical in every respect (Emmons,[13] Spring [14]).

CHLAMYDOSPORES

In many strains of dermatophytes chlamydospores are produced in great numbers. They are numerous in Epidermophyton floccosum, T. violaceum, T. Schoenleini and others, but since they also appear in great numbers in some strains of other species their use in the differentiation of species is limited. Chlamydospores are abundant even in strains of T. mentagrophytes, in which sporulation by conidia is well developed. The chlamydospores are larger than the conidia, are usually intercalary and are usually large rounded cells in which there is a concentration of protoplasm and food material (fig. 5). They are to be found

12. Neto, V. B., and Martins, C.: Mycose des ongles et epidermophyton nigricans, Ann. de dermat. et syph. **4**:526, 1933.

13. Emmons, C. W.: Observations on Achorion Gypseum, Mycologia **23**:87, 1931.

14. Spring, D.: Heterothallism Among the Dermatophytes, Arch. Dermat. & Syph. **24**:22, 1931.

on or in the agar after the mycelial layer has been peeled back. They are not peculiar to the ringworm fungi and cannot be considered to have great taxonomic value.

SPIRALS

Besides the spores certain other characteristic structures are to be found in the dermatophytes. In T. mentagrophytes tightly coiled hyphae often appear (fig. 12). These coiled hyphae, the "spirals," have been looked on by many as related in some way to the perfect, that is, to the ascocarpic phase of these fungi. Until these structures are found actually to be associated with asci in the dermatophytes there is no adequate reason for looking on them as anything but strictly vegetative structures. They are not like the spirally coiled hairs which adorn the ascocarp of some species of Chaetomium. The latter are dark, with thick, rough walls, and rise directly from the perithecium. The spirals of the dermatophytes have smooth thin walls and develop as specialized branches from the vegetative hyphae. Like some other structures produced by the fungi, they are not believed to possess any particular function or evolutionary significance.

The presence or absence of these spirals has been used to delimit certain species. As a matter of fact, they are to be found in several species of dermatophytes. Besides their common occurrence in many strains of T. mentagrophytes they are also to be found in other species and genera. They have been reported by Langeron and Milochevitch [6] in the endothrix trichophytons, in Epidermophyton floccosum and in the animal Microsporum when grown on cereal grains. They appear in M. gypseum when it is grown on nail parings (Emmons [13]). As a matter of fact, spirals occasionally appear in M. felineum even when it is grown on Sabouraud's maltose agar (fig. 21).

ANTLER-LIKE HYPHAE

More suggestive of the perithecial structure known in certain of the Gymnoasceae, with which family the dermatophytes appear to show affinities, are certain stiff, curved, freely branching, antler-like hyphae associated with the formation of masses of conidia in some strains of T. mentagrophytes (fig. 13). These peculiar branches become encrusted (fig. 14), as Langeron and Milochevitch [6] have pointed out. The conidia develop, not on these ultimate branches, but from the hyphal cells at the center of the complex which bear both the conidia and the antler-like branches (fig. 13). The conidial masses are conspicuous features of growth in some strains and have the gross appearance of the ascocarps of Gymnoascus. The stiff, curved, branching hyphae which are in and around these masses add microscopically to the resemblance. However, asci are not present. Until they can be demonstrated there is not

sufficient justification for calling these structures perithecia, even though they be specified as sterile perithecia (Langeron and Milochevitch[6]). Langeron and Milochevitch, in characterizing the family Gymnoasceae, stated, "Asques arrondis, octosporés, naissant sur les prolongements internes des filaments qui constituent le périthèce." (Round octosporous asci arising on the internal prolongations of the filaments which form the perithecium.) In reality the asci in the Gymnoasceae as well as the conidia in Trichophyton develop centripetally from the base and not inward from the hyphae forming the perithecium of the ascocarp. It may be that this misconception is responsible for the willingness of Langeron and Milochevitch to pronounce the conidial masses of the Trichophytons "perithecia."

NODULAR ORGANS

The most interesting structure formed by the dermatophytes and the one which gives the strongest evidence of a relationship with the Ascomycetes is the "organe nodulaire." It bears a strong resemblance to the ascogonium seen in many of the lower Ascomycetes and will be so designated in this study. It begins as a slightly swollen side branch or terminal cell of a hypha (fig. 11 *A* and *C*). Occasionally it consists of one or more intercalary cells in a hypha (fig. 11 *B* and *D*). It may be picked out not only by its morphologic characters but also by its staining reaction (at least when young) to acetocarmine[14a] which stains it selectively. It becomes curved and may coil on itself (fig. 11 *E*) around a vegetative or sporulating hypha (fig. 11 *H* and *F*) or around a second specialized branch (fig. 11 *G*). Septums may appear, and in some strains there is no further development. In others the cells of the coil may proliferate and form a small knot of hyphae. However, one looks in vain for further development into a fertile ascocarp. The reason for the abortion of a structure which has every appearance of an ascocarp primordium remains unknown. It may be a deficiency in the conditions of the culture, or it may be that the fungus is heterothallic, that is, with the sexes (if one may so designate them) segregated in different individuals so that the presence of both is required for fertilization. This is a condition well known in some fungi. If the former is true these fungi ought to produce ascocarps on some of the great variety of mediums, either natural or synthetic, on which they have been grown by different investigators. The latter is an attractive possibility but is somewhat discredited by two lines of evidence. Many other fungi, presumably related to the dermatophytes are homothallic, that is, have

14a. To prepare the acetocarmine stain 45 per cent glacial acetic acid to which an excess of carmine has been added is heated to boiling, cooled, and filtered. The object to be examined is mounted in this solution under a cover slip and examined at once.

both of the sexual elements in the same individual. In the second place an extensive series of attempted matings have not yielded ascocarps.

In an attempt to learn whether the pairing of different strains would be effective in inducing the formation of asci over 300 matings of dermatophytes were made in plate cultures. In this series 42 strains including 25 species (as defined by Sabouraud) were paired in various

Fig. 26.—Two strains of T. mentagrophytes. At the line where the two colonies meet there is an increase in the number of ascogonia (nodular organs).

combinations. The strains used included not only strains isolated in this laboratory, but also strains from Dr. Sabouraud's collection which he sent us. The problem of geographic species was therefore included. Plate cultures were used, and the medium, the distance between the points of inoculation, the temperature of incubation and the illumination were varied. Additional attempts at pairing were made in about 100 cases by putting spore suspensions of given strains on well developed colonies of other strains. No asci were found at any time, but in the former series the interesting observation was made that in certain com-

binations, particularly in those involving 2 strains of T. mentagrophytes, there was an increase in the aerial mycelium along the line where the two mycelia met, as shown in figure 26. Ascogonia were formed profusely within this mycelial growth. Both strains when grown alone produced some ascogonia, but when they were grown together in this manner there was a marked increase in their numbers. This was observed in 75 pairings. The phenomenon was observed early in the series so that these two fungi were used more often than others, either against each other or with other strains. One of these was a strain of T. mentagrophytes obtained from Dr. Sabouraud; the second was a strain of the same species described elsewhere (Emmons[15]). Since both strains produced some ascogonia when grown alone, and since the development of asci did not follow their formation this cannot be presented as evidence for a heterothallic condition in these fungi.

The occurrence of ascogonia is rather sporadic. If absent from the aerial mycelium they can be found in some cultures at the surface of the culture medium or even submerged in it. They occur commonly in many strains of T. mentagrophytes, and are present in considerable numbers in some strains. They are to be found also in the variety usually called Trichophyton interdigitale, in M. gypseum, in M. felineum, and in Schoenleini. Their production by these different species is further evidence of the close relationship of the different dermatophytes.

PRODUCTION OF PIGMENT

The ability to form characteristic pigments has been used to delimit certain species. In certain cases this is a useful criterion. The production of pigment, however, is such a variable character that its usefulness is limited. T. violaceum usually loses its pigment-producing ability after successive transfers. The same is true of some strains of Trichophyton sulfureum. Many strains of T. mentagrophytes produce a brown to wine-colored pigment visible in zones in the reverse of the colony. In certain subcultures its amount may be either increased or decreased. Variants from a single spore strain of such a species may vary greatly among themselves in this respect. Pigmentation may be visible in the aerial mycelium, and some species produce diffusible pigments.

CLASSIFICATION

The classifications of the dermatophytes which have been recently proposed have brought confusion rather than clarity. They have been presented as botanical classifications based on morphologic grounds, but by separating related forms and by bringing together diverse forms

15. Emmons, C. W.: Variants and the Validity of Species in Some Dermatophytes, Bol. Asoc. méd. de Puerto Rico **24**:591, 1932.

they fall short of this ideal. No reclassification can detract from the value of Sabouraud's monumental work on these forms. The need for stabilization in the nomenclature is well illustrated, however, in one of Sabouraud's [16] recent contributions in which, without definition or explanation, he uses certain specific names as though they were generic names.

It is generally admitted the ideal classification for these forms is a mycologic one, that is, a classification based on the morphologic characters of these fungi in culture. At the same time it is commonly stated that these fungi do not lend themselves to such a classification, and that when one is imposed on them its lines cut across those of the previously used clinical classification. In my opinion, the dermatophytes are as amenable to a mycologic classification as other groups of the fungi imperfecti, and such a classification runs counter to the clinical groupings of the Sabouraud school in minor points only.

Sabouraud [17] has briefly reviewed the clinical features on which his classification rests. When one examines the fungi responsible for the different types of lesions one finds that a mycologic grouping coincides fairly well with this clinical grouping. The classification proposed here differs from that of Sabouraud mainly in that it places the emphasis on the morphologic features of the fungus in culture. Consequently there is no radical departure from the familiar classification, but it has been possible to avoid certain inconsistencies which marred its usefulness.

One of the inconsistencies of Sabouraud's clinical classification arises because a given fungus does not always produce the same type of lesion, nor is a given type of lesion always caused by the same fungus. Sabouraud [18] pointed out that the favus "godet" may be lacking in infections due to A. Schoenleini, the common cause of favus, and that it may be caused by an endothrix (Achorion violaceum) or by an animal Microsporum (A. gypseum). Furthermore, the line between ectothrix and endothrix species is crossed when a culture becomes "pleomorphic" (Langeron and Talice,[19] Catanei [20]). Catanei [21] stated

16. Sabouraud, R.: Généralities concernant les dermatophytes, Ann. de dermat. et syph. **10**:481, 1929.

17. Sabouraud, R.: Généralities concernant les dermatophytes, Ann. de dermat. et syph. **10**:236 and 569, 1929.

18. Sabouraud, R.: Généralities concernant les dermatophytes, Ann. de dermat. et syph. **9**:656, 1928.

19. Langeron, M., and Talice, R. V.: Nouveau type de lésion pilaire expérimentale produite par la culture purement pléomorphique du Sabouraudites felineus, Ann. de parasitol. **8**:419, 1930.

20. Catanei, A.: Sur le parasitisme des poils dans l'infection experimentale provoquée par des cultures pléomorphique d'un Trichophyton gypseum, Compt. rend. Soc. de biol. **105**:348, 1930.

21. Catanei, A.: Caractères du parasitisme pilaire dans les teignes expérimentales produites par les cultures pléomorphiques des dermatophytes, Compt. rend. Soc. de biol. **109**:1105, 1932.

that, in general, when an infection is caused by the pleomorphic form of an endothrix species it shows reduced parasitism; when it is caused by the pleomorphic form of an ectothrix species, it exhibits the type of invasion characteristic of the endothrix variety.

There appear to be three natural groups of dermatophytes: 1. There are species of Trichophyton which reproduce in culture principally by subspherical to clavate conidia and also form in many if not all species smooth, thin-walled, few-celled, clavate macroconidia. In hairs infected by species of Trichophyton the arthrospores into which the hyphae become cut are more or less definitely in rows. There are three sub-

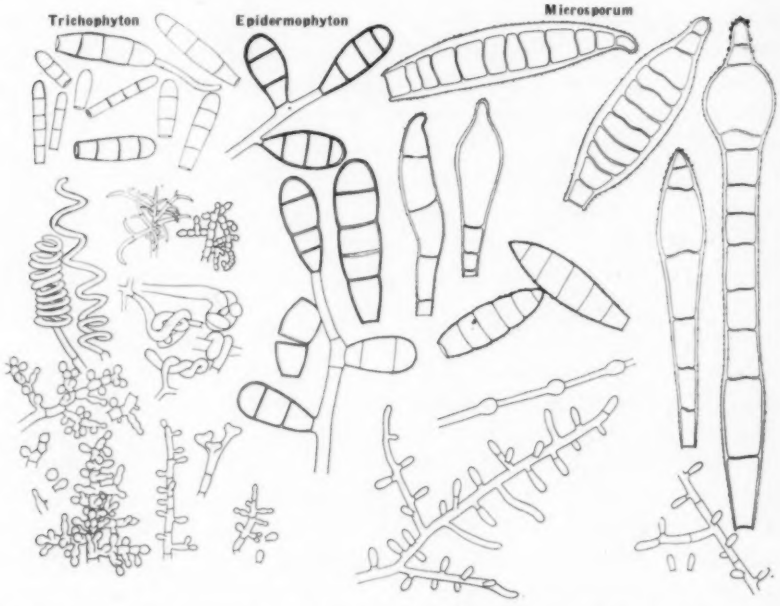


Fig. 27.—Tabular arrangement of spores and other organs in the three genera of dermatophytes.

groups, according to clinical manifestations, which coincide roughly with three types of Trichophyton cultures.

2. The second group comprises Epidermophyton with at least one distinct species, Epidermophyton floccosum (Epidermophyton inguinale), which reproduces in culture exclusively by oval to egg-shaped macroconidia which are smooth and thick-walled, with from two to a few cells. Clinically, an infection by Epidermophyton cannot always be distinguished from an infection by Trichophyton, but as the former occurs in typical lesions in the axillae and in the groin it is a definite clinical entity. It does not invade the hair. Species of Endodermophyton and some species of Trichophyton which are ordinarily found on the

glabrous skin invade the hair, however, in experimentally infected guinea-pigs (Ota and Kawatsuré,[7] Catanei [21]).

3. There are finally species of Microsporum which reproduce in culture principally by spindle-shaped macroconidia (except in M. Audouini and its varieties in which the macroconidia are few and abortive) and also produce clavate conidia. In hairs infected by species of Microsporum there is a characteristic sheath around the hair in which the arthrospores are arranged as in a mosaic.

In this enumeration favus and its causal fungus have, so far, been omitted. Common favus is caused by one species which has been called Achorion Schoenleini.[21a] Infection by this fungus usually causes a definite clinical picture. However, some of the clinical features of favus may be caused by other fungi. As Sabouraud has pointed out, the fungi which occasionally cause favus show affinities with species of Microsporum of animal origin and with endothrix species of Trichophyton. A. Schoenleini is mycologically a species of Trichophyton. The classification is simplified by omitting the generic name Achorion. The principal species, A. Schoenleini then becomes T. Schoenleini, and the others fall into their respective groups. This step ends the confusion arising in cases such as that in which the same fungus is called A. gypseum when it is isolated from a favus-like lesion, and Microsporum fulvum when it comes from another type. This step is recommended by Langeron and Milochevitch.[6] The generic name Endodermophyton is likewise discarded because its species are referable to the Trichophyton group.

There appear to be adequate reasons for accepting these three genera and excluding others. The generic term Trichophyton was created in 1845 by Malmsten [22] for the species Trichophyton tonsurans (Trichophyton crateriforme). It should comprise all the species which reproduce in culture by the Trichophyton type of conidia and macroconidia as heretofore described. In species lacking one of these organs, other characters can be depended on to indicate relationship.

The record of Epidermophyton is not so clear. In 1879 Lang saw certain bodies in scales from psoriasis which he believed to be of mycotic nature and applied to them the name Epidermidophyton. These bodies were artefacts. Two years later, Mégnin [23] studied a disease of the comb and skin in fowls and named the fungus causing it Epidermophyton gallinae. He does not refer to the earlier name, and his spelling is sufficiently different to allow the term Epidermophyton

21a. The first use of the specific name Schoenleini is that of H. Lebert (Physiologie pathologique, Paris, J.-B. Baillière, 1845, vol. 2, p. 490).

22. Malmsten, P. H.: Trichophyton tonsurans, Arch. f. Anat., Physiol. u. Wissensch. Med., 1848, p. 1.

23. Mégnin, P.: Nouvelle maladie parasitaire de la peau chez un coq, Compt. rend. Soc. de biol. **3**:404, 1881.

Mégnin to stand. However, Sabouraud, because of certain clinical characters of the disease in fowls called the fungus causing it Achorion gallinae, and in 1907, without referring to either of the earlier investigators, he applied the name Epidermophyton inguinale to the very different fungus which causes eczema marginatum. This use of a generic name for a species differing essentially from the type species of the genus, a type species, moreover, which has been transferred to another genus, is a violation of the rules of nomenclature. The name, however, is well established in the literature, and rather than create a new genus to supplant it it is used here in the sense of Sabouraud. Sabouraud must therefore be considered the author of the generic term since he used the name in a sense quite different from that of Mégnin. It may be that eventually this name will have to be supplanted in order to conform to the rules of nomenclature, but no change from the established usage is made at this time. The genus as now understood contains one species, Epidermophyton inguinale Sabouraud, and perhaps no others. This one species had already been observed and described clinically and in culture by Harz [24] in 1871 under the name Acrothecium floccosum. It was shifted to Acrothecium and then to Blastotrichum, as Rabenhorst lists it. Its habitat and morphology amply justify its removal from that genus. Since 1905 it has been described in the medical literature under several different specific names. Langeron and Milochevitch [6] and Ota [25] list the terms used synonymously for this species, but their statement regarding the authorship of the generic name is not entirely correct. The name of this fungus becomes Epidermophyton floccosum (Harz),[24] Langeron and Milochevitch.[6]

The genus Microsporum was set up in 1843 by Gruby,[26] and, as used by Sabouraud, includes a number of related species producing in culture large, thick-walled macroconidia. Attention should be called to the spelling of this name. In his original description Gruby gave the spelling as "Microsporum," and this should be retained. This is the spelling used by Sabouraud. Some English and American writers have incorrectly altered the name to "Microsporon," and the German usage is "Mikrosporon." Ota and Langeron [2] discarded this genus, distributing its species in the genus Trichophyton and in their new genus, Sabouraudites. This resulted in the separation of related species and

24. Harz, C. O.: Einige neue Hyphomyceten Berlin's und Wein's nebst Beiträge zur Systematik derselben, Bull. Soc. imp. d. natural. de Moscou **44**:88, 1871. Harz had previously reported this species as Tricothecium Floccosum (Harz: Ztschr. d. allg. öster Apoth. Ver., 1870, no. 23).

25. Ota, M.: 1931. Epidermophyton-Epidermidophyton, Ann. de parasitol. **9**: 277, 1931.

26. Gruby, D.: Recherches sur la nature, le siége, et le development du porrigo décalvans ou phytoalopécie, Compt. rend. Acad. d. Sc. **17**:301, 1843.

in the bringing together in the genus Sabouraudites of species differing in morphologic characters. Conservation of the genus for species reproducing by large, spindle-shaped macroconidia and obviously related species in which the macroconidia are of the same type but may be few and abortive follows natural lines more closely.

Considering, then, that favus is caused by a particular species of Trichophyton, and considering "Endodermophyton" a synonym of "Trichophyton," there are three groups of dermatophytes. These three groups or genera of fungi manifest their close relationship by their methods of reproduction in culture. The three groups are differentiated by the distinctive types (not by the relative numbers) of macroconidia which they form in culture. When one or the other type of spore is absent in a strain one must look to other characters for classification, but in general the conidia indicate a close relationship between species of the dermatophytes, and the characters of the macroconidia set apart three groups represented by the genera Trichophyton, Epidermophyton and Microsporum.

The points presented in support of this classification are that it follows natural lines of relationship; because it is a natural or mycologic classification it is simpler than others which have been proposed; by creating no new generic names it does less violence to the old familiar nomenclature, and finally, in redefining the old generic names and shifting the emphasis from the clinical aspects of the disease to the cultural characters of the fungus it is not proposing something radically different but is in fact restoring the original concepts of the genera. Microsporum, for example, was so named by Gruby because of the small size of the mycelial spores around the hair, and the fungus should be further defined in terms of the fungus, not of the clinical picture of the disease which it causes. The other genera also appear to have been described with the fungus and not with the disease primarily in mind. The diseases are set apart by their own distinctive names.

In order to present in the usual precise form description of the group and of the genera the following brief definitions are suggested:

Dermatophytes.—These fungi are Hyphomycetes. They are usually white, but in some species show some shade of yellow, pink, violet or brown; they reproduce by arthrospores, by chlamydospores, by single-celled conidia which are subspherical or pear-shaped to clavate, with broad bases, the base often being surrounded by a collar marking the point of attachment of the spore, borne singly along the hyphae or in clusters on specialized conidiophores, sessile or stipitate, sometimes forming chains of two or three spores, and measuring 2.5 to 4 by 3 to 6 microns. They also reproduce by macroconidia which are clavate to spindle-shaped, or occasionally one-celled, but usually have from one to many cross-walls, and measure up to 40 by 150 microns in some

species. They grow in the skin and its appendages, where they are present only as mycelia or arthrospores.

Trichophyton Malmsten 1845.—The type species is T. tonsurans Malmsten 1845. The mycelium is usually white, but in some species it is yellow, pink, violet, or brown. The organisms reproduce in culture principally by conidia. The macroconidia are clavate, thin-walled and sometimes wanting.

Epidermophyton Sabouraud 1907 (not Lang 1879 or Mégnin [23] 1881).—The type species is Epidermophyton inguinale Sabouraud 1907, which corresponds to Epidermophyton floccosum (Harz [24] 1870) Langeron and Milochevitch.[6] The mycelium is usually yellow; the organisms reproduce in culture by chlamydospores and by oval to egg-shapped, smooth, thick-walled macroconidia.

Microsporum Gruby [26] *1843.*—The type species is M. Audouini Gruby 1843. The mycelium is usually from white to brown; the organisms reproduce in culture principally by spindle-shaped, thick-walled macroconidia and clavate conidia. The former may be abortive or few in some species.

The synonymy indicated in the following list is for the most part that which has already been suggested by Langeron and Milochevitch, Ota and Kawatsuré and others. The limits of the species T. mentagrophytes have been here further extended to include the T. niveum group. A more complete study and report on this phase of the problem is in progress.

PARTIAL LIST OF THE SYNONYMY OF THE DERMATOPHYTES

Trichophyton Malmsten 1845

T. tonsurans Malmsten 1845
  T. crateriforme
T. Schoenleini (Lebert 1845) Langeron and Milochevitch 1930
  Achorion schoenleini
T. mentagrophytes (C. Robin 1853) Blanchard 1895
  T. gypseum, T. asteroides, T. granulosum, T. radiolatum, T. lacticolor, T. farinulentum, T. persicolor, T. interdigitale, T. pedis. T. niveum, T. denticulatum, T. radians, T. felineum·
T. Megnini Blanchard 1895
  T. roseum, T. rosaceum
T. concentricum Blanchard 1895
  Endodermophyton concentricum, Endodermophyton tropicale, Endodermophyton indicum
T. Sabouraudi Blanchard 1895
  T. acuminatum

T. violaceum Sabouraud 1902
T. glabrum, Achorion violaceum
T. epilans Boucher and Mégnin 1887
T. flavum, T. cerebriforme
T. sulfureum C. Fox 1908
T. album Sabouraud 1909
T. ochraceum, T. discoides
T. rubrum Castellani (1909) Sabouraud 1911
T. purpureum, Epidermophyton rubrum, Epidermophyton salmoneum
T. ferrugineum (Ota 1921) Langeron and Milochevitch 1930
Microsporum ferrugineum

Epidermophyton Sabouraud 1907

E. floccosum (Harz 1870) Langeron and Milochevitch 1930
Tricothecium floccosum, Acrothecium floccosum, Blastotrichum floccosum, Trichophyton intertriginis, E. inguinale, E. cruris

Microsporum Gruby 1843

M. Audouini Gruby 1843
M. velveticum, M. umbonatum, M. tardum, M. depauperatum
M. equinum (Bodin 1898) Sabouraud 1910
M. gallinae (Mégnin 1881) Grigorakis 1929
Epidermophyton gallinae, Achorion gallinae
M. quinckeanum (Zopf 1890) Guiart and Grigorakis 1928
Achorion quinckeanum
M. felineum Mewborn 1902
M. lanosum
M. gypseum (Bodin 1907) Guiart and Grigorakis 1928
M. fulvum, Achorion gypseum

SUMMARY

Present classifications of the dermatophytes are unsatisfactory. Recent attempts to substitute a botanical for the clinical classification have not been successful because of the failure to recognize proper criteria for a natural grouping. Morphologic studies have indicated certain natural lines of separation in the group.

A small culture cell, which is described, was used to supplement plate and tube cultures in studying the development of conidiophores and conidia.

The spores are conidia and macroconidia, not aleuries and fuseaux. The conidia vary in size and shape, but these variations may exist within

a single species. The conidia of the dermatophytes are characteristic. The manner of spore formation is compared and contrasted with that of certain other fungi. The subterminal elements of the branching conidiophore-like structure are really spores; that is, the fungus forms short chains of spores.

The form of the conidium indicates a close relationship between the different species and genera of the ringworm fungi. The macroconidia are of three types; those of species of Trichophyton are clavate and thin-walled, and have few cross-walls; those of Epidermophyton are clavate to egg-shaped and thick-walled, and have few cross-walls; those of Microsporum are spindle-shaped and thick-walled, and in some species have as many as fifteen cross-walls. The type of macroconidium serves to differentiate these three genera, which as here defined represent three natural mycologic groups of dermatophytes.

The generic names Trichophyton and Microsporum are retained by right of priority, and Epidermophyton (in the sense of Sabouraud) is retained because of established usage. The genera Achorion and Endodermophyton are unnecessary, their species being distributed among the accepted genera, and because they are fertile sources of confusion they should be rejected.

Chlamydospores and spirals are of little taxonomic value. The "nodular organs" are formed by many species and are probably ascogonia. In a series of attempted matings the number of ascogonia was increased at the line of junction between certain pairs. This is not regarded as evidence of heterothallism.

The dermatophytes can be classified mycologically. Such a natural classification follows in a general way Sabouraud's clinical classification. The inconsistencies of that classification can be avoided by shifting the emphasis from the clinical to the mycologic aspects. This is not an innovation but restores the original concepts of the genera. It permits the retention of three familiar generic names.

The three natural groups of dermatophytes and the points which characterize them are discussed. The authorship of the genera is enumerated, and the characters of the three genera are set down. A partial list of the synonymy is given.

This classification is proposed in the belief that it follows natural lines of relationship and will therefore, if accepted, bring stability to the nomenclature of the dermatophytes. It restores to three ancient genera a mycologic definition, which, to some degree at least, seems to have been the intent of the authors of the names. Finally, because it coincides so nearly with the clinical classification which has been made familiar to dermatologists by Dr. Sabouraud's extensive researches and able presentation it is expected that its acceptance will cause a minimum of confusion.

SARCOMA IDIOPATHICUM MULTIPLEX HAEMORRHAGICUM (KAPOSI)

VARIATIONS FROM THE USUAL CLINICAL PICTURE

JAMES R. WEBSTER, M.D.
CHICAGO

Under the title "Idiopathic Multiple Pigment Sarcoma of the Skin," Kaposi [1] first described, in 1872, the disease which is now associated with his name. In 1894 he changed the designation to "sarcoma idiopathicum multiplex haemorrhagicum," to indicate better the source of pigment in the lesions. In his classic descriptions he mentioned the symmetry and multiplicity of the lesions from the onset as characteristic for the condition.

Since that time many variations from the original picture have been noted by various observers, but there have been relatively few cases reported in which, through a fairly long course, the disease remained unilateral and restricted to one or a small group of lesions. In this connection the case reported here, which was presented before the Gesellschaft der Aerzte in Vienna on Jan. 8, 1926,[2] is interesting in that, although the condition was present for six years, death from other causes intervening, the manifestations remained restricted to one hand with only slight encroachment on the forearm.

REPORT OF A CASE

History.—C. K., a 77 year old Polish Jew, was admitted to the dermatologic division of the Krankenhaus der Stadt Wien on Dec. 15, 1925. The family history was without significance. The patient had contracted syphilis in 1878, and since then he had received two courses of mercurial inunction therapy. Since 1923 alterations of the skin of the right hand had been present which finally induced him to seek medical aid. In the beginning the skin of the back of the hand had become somewhat thickened. As time passed this thickening spread to the fingers, and the skin became bluish and uneven. The patient could give no information as to the time of appearance of certain vascular ectasias on the left hand.

Examination.—At the time of admission the subcutaneous fatty tissue was reduced. The prostate was considerably enlarged, the right lobe especially being firm and tender. In addition there was a large scrotal hernia. Aside from these findings, the general examination as well as urinalysis revealed nothing abnormal.

Dermatologic Observations.—As a result of the changes present in its cutis the right hand, in its entirety, was considerably larger than the left (fig. 1). The

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From the dermatologic division of the Krankenhaus der Stadt Wien; Prof. Dr. Otto Kren, chief of staff.

1. Kaposi, M.: Arch. f. Dermat. u. Syph. **4**:265, 1872.
2. Kren, O.: Wien. klin. Wchnschr. **39**:85, 1926.

dorsum of the hand was the seat of a bluish to brownish-violet, rather diffuse thickening of the skin, extending proximally practically to the wrist and distally over the proximal phalanges. In the case of the fourth finger, the changes extended to the tip. The increase in size of the proximal phalanges thus produced was of such magnitude that, with these approximated, the tips of the fingers remained a considerable distance apart. Changes similar to those on the dorsum were also present on the distal third of the palm and contiguous portions of the fingers. The transition from normal to diseased skin was gradual, the thickening being most marked on the dorsum of the hand over the third and fourth metacarpal bones. Palpation revealed that in the affected area, in addition to edema, there was a rather diffuse infiltration, in general of a firm consistency, but in places somewhat elastic. Scattered in the infiltrated region, most numerous toward the center, were many firm reddish-brown nodules ranging in size from that of a hemp

Fig. 1.—Dorsal view showing the extent and distribution of the lesion on the right hand.

seed to that of a pea, some lying within the skin, others projecting somewhat above its level. Toward the periphery of the lesion a few such nodules could be found, but here the infiltrate was more definitely flat and diffuse, gradually tapering off into the normal skin. On the palmar surface of the hand and fingers were a few small, circumscribed areas of hemorrhage from light brown to black in the more superficial layers of skin. There was slight adherent scaling on the dorsal surface of the fingers and the distal portion of the dorsum manus, but otherwise the surface was little altered, and there was no ulceration at any point. Roentgenologic examination of the hand on Jan. 2, 1926, revealed no pathologic process of the bones or joints.

The lower part of the right forearm was definitely swollen and edematous as compared with the left, and the veins were more prominent. A few small, isolated nodules, similar to those on the hand, could be palpated. Aside from these there were no other lesions of this type on the skin or in the visible mucous membranes.

In the right axilla was a small moderately firm, palpable but not tender gland the size of a grape. No other significant evidence of adenopathy was found.

On the flexor surfaces of the proximal and middle phalanges of the second to fifth fingers of the left hand, and to a lesser extent on the first phalanx of the thumb, was an unusually prominent venous network. The vessels showed blue-green through the skin, and could not be completely emptied by pressure since in places they widened out somewhat, forming cavernous convolutions. A few bluish-green streaks were visible on the palm. The distal phalanges and the dorsum of the hand in general appeared normal.

Microscopic Observations.—On Dec. 21, 1925, a piece of tissue was excised from the dorsum of the right hand, fixed in alcohol and embedded in paraffin, and the sections stained by various methods.

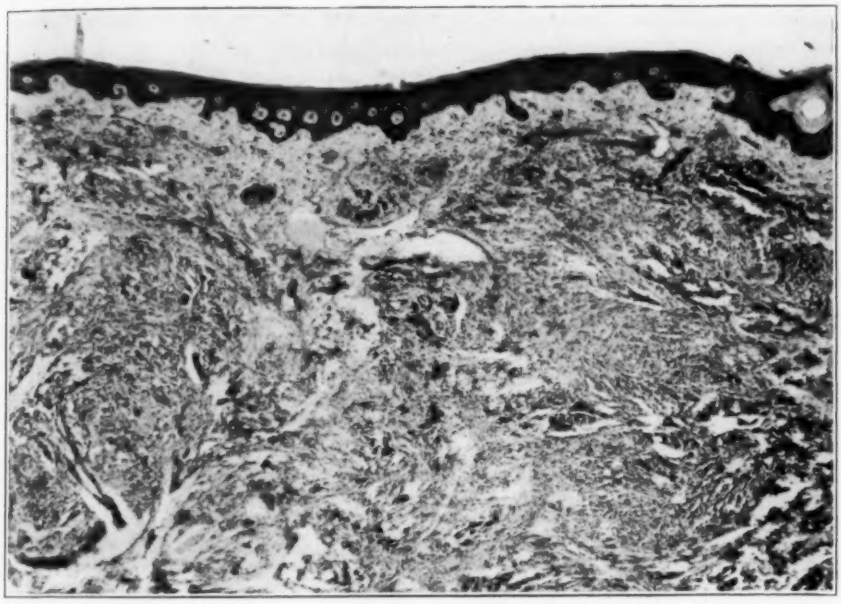

Fig. 2.—Low power photomicrograph showing the intermediate zone under the epithelium, ectatic blood and lymph channels and intervening tissue containing many spindle cells.

Sections stained with hematoxylin and eosin revealed moderate hyperkeratosis and slight acanthosis. In places, though not throughout the sections, there was an increased amount of dark brown pigment present in the basal layer of the epithelium. Aside from these there were no noteworthy changes in the epithelium.

The corium as a whole was much thicker than normal. Directly under the epidermis was a narrow zone relatively free from changes, showing only moderate vascular dilatation with slight perivascular infiltration of small lymphocytes and a few plasma cells. Under this zone were the characteristic changes, involving the greater part of the corium. There were two main components of the pathologic picture: first, greatly dilated blood and lymph spaces of capillary type with evident proliferation, and, second, cellular interstitial tissue of round and spindle cells, chiefly the latter (fig. 2). The demarcation of this tissue, both above and

into its vague nodular configurations, was not sharp, but nevertheless quite definite, for at the borders one found that the vessels were the most prominent feature, while centrally the spindle and round cells were more numerous. In addition there was considerably more pigment in the peripheral regions than in the center.

The blood capillaries toward the margins appeared as round, ectatic spaces the endothelial cells of which were swollen and at times of more than one layer. The lymph spaces, recognizable as such because of fewer endothelial cells and a granular eosinophilic content, were as a rule larger and more irregular as to shape. Around these vessels were a few lymphocytes and plasma cells with an occasional eosinophil, in addition to many granules and clumps of a golden brown pigment which gave a positive prussian blue reaction for iron. Spindle cells could also be found in small numbers between these vessels, but in the more central regions they were much thicker. Here, along with round cells they were densely packed about vascular spaces of the aforementioned types, so that in places it was impossible to differentiate between vascular endothelium and surrounding spindle cells. There was a tendency for the latter to be grouped in bundles running along and around the vessels and interlacing with one another. In places, however, narrow, apparently compressed, parallel vessels seemed to penetrate a solid mass of spindle cells the nuclei of which varied considerably in shape, size and staining qualities, mitotic figures being not uncommon. These cells were so tightly packed together that little intercellular collagen was demonstrated by hematoxylin and eosin or van Gieson's stain. With the lithium carmine-Weigert method the elastic fibers were found to be completely missing in the regions of most dense spindle cells, fragmented and rarefied in other regions, and relatively normal in the subepithelial zone. Red blood cells could occasionally be seen outside vascular channels, but not clearly, because of the alcohol fixation.

In summary, then, one found a pathologic tissue, arising in the corium, composed of ectatic and proliferating blood and lymph spaces, surrounded by a cellular mass rich in spindle cells which might possibly have risen from vascular endothelium. Scattered throughout the mass, but most noticeable in the more richly vascular regions, were evidences of old and recent localized hemorrhages.

Course.—The patient was given roentgen radiation, in the dosage of 300 roentgens, on December 31 and January 14. Two days after the second irradiation definite regression of the tumor could be observed. The areas that had been somewhat elastic before were now considerably firmer, and the nodular elevations were much flattened. Irradiation in the same dosage was repeated two weeks later. On February 9 the skin in the affected region had attained nearly normal thickness and the bluish-red to brown-violet color had largely disappeared, replaced by a dark brownish tint. The patient was discharged from the hospital, to be treated further in the ambulatory clinic.

After having four more treatments at intervals of two weeks, the last on April 4, continued improvement was noted, and the patient disappeared from observation. On Dec. 17, 1929, the patient died in another hospital. Myocardial degeneration was given as the cause of death. The condition of the skin at the time of death was much the same as when last seen, although a few new nodules had developed on the right forearm just above the wrist. No other traces of the disease were found anywhere in the body.

COMMENT

It cannot be doubted, in view of the clinical appearance of the cutaneous manifestations together with their histologic picture, that this

was a case of Kaposi's sarcoma. Yet here is an instance of the disease remaining localized to one hand, with only slight extension up the forearm over a period of six years, without dissemination. Treatment was given only during a period of slightly over three months in the middle of this period. While such a condition is not characteristic of the disease as originally described, it must be recognized that it may be encountered, with progression and bilateral distribution delayed for some time, or possibly not seen if death from other causes intervenes.

The prominent venous network on the palmar surface of the left hand and the enlarged veins on the right forearm were of additional interest. It is not uncommon for dermatologists to observe, on the trunk or extremities of patients suffering from this condition, small, localized areas of telangiectasia which later develop into typical lesions of the disease. Saphier [3] called attention to the extension of Kaposi's sarcoma along the course of blood vessels. In his case, in addition to typical cutaneous lesions, there were, on the legs, deep-seated, bluish-green, branching streaks which in places widened out in the manner of varicose veins and were firm and palpable through the skin. Histologically the smallest of these streaks were found to be cavernous vessels without accompanying change. However, those of diameter larger than from 2 to 3 mm. showed aggregations of spindle cells closely packed about many small blood spaces, with some pigment deposited in the region. When such a region was followed in serial section it was found that the blood spaces became confluent and terminated in a thin-walled vein, without spindle cell mantle, at the point at which the streak narrowed.

In the light of such facts it is conceivable that the enlarged veins on the right forearm of my patient represented propagation of the disease, and that the venous network on the left hand was a prodromal manifestation, presaging the appearance there, at a later date, of typical cutaneous lesions had the patient not died.

A few cases similar to this, in which one or a few lesions appeared and remained for a considerable period of time as the sole efflorescence, have been recorded. For example, Selhorst and Polano [4] reported a case of a small rose-red spot on the left hand which largely disappeared on pressure. For about eighteen years the disease apparently remained stationary, after which there was a relatively rapid extension, so that, at the time of observation, twenty years after the onset, both hands and feet presented lesions that were clinically and histologically typical. Kreibich,[5] in an article devoted chiefly to granuloma pyogenicum, presented a case of Kaposi's sarcoma in which there were but two cuta-

3. Saphier: Arch. f. Dermat. u. Syph. **118**:671, 1913.

4. Selhorst and Polano: Arch. f. Dermat. u. Syph. **82**:33, 1906.

5. Kreibich: Arch. f. Dermat. u. Syph. **94**:121, 1909 (case 6).

neous lesions, both on the right foot. Gilchrist and Ketron [6] observed a case in which there were six localized lesions on the face, the oldest of two years' duration, which were proved to be multiple idiopathic hemorrhagic sarcomas and which were cleared up by roentgen therapy. Brann and Seuffer [7] reported a case from the clinical records and moulages of Frieboes, in which the lesions were almost entirely restricted to the right hand, there being only slight involvement of the left, and none of the rest of the body. In Mierzecki's case 6,[8] the manifestations of the disease were confined to the right hand and elbow when the patient was observed after two years' duration. Cattaneo [9] observed two patients, in each of whom there was but a single lesion, in one on the right leg and in the other on the left. In the case of Senear and Wien,[10] the manifestations of the disease were restricted to the left foot and ankle.

SUMMARY AND CONCLUSIONS

1. A case of sarcoma idiopathicum multiplex haemorrhagicum (Kaposi) is reported in which only the right hand and, to a slight extent, the right forearm were affected for six years. Death from other causes occurred at the end of that time.

2. Along with a relatively few similar cases this indicates that, aside from the type originally described by Kaposi, the condition may be encountered with a single or a few localized efflorescences, frequently on only one side of the body, which remain for an extended period before extension occurs.

3. In such cases, as well as in those conforming to the classic type, the diagnosis may be reached through a study of the clinical appearance of the lesions, their histologic picture and the course of the disease.

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6. Gilchrist and Ketron: J. Cutan. Dis. **34**:429, 1916 (case 2).
7. Brann and Seuffer: Arch. f. Dermat. u. Syph. **141**:69, 1922 (case 2).
8. Mierzecki: Arch. f. Dermat. u. Syph. **165**:577, 1932.
9. Cattaneo: Boll. sez. region. Soc. ital. dermat., 1933, no. 1, p. 84.
10. Senear, F. E., and Wien, M. S.: Multiple Idiopathic Hemorrhagic (Kaposi) Sarcoma, Arch. Dermat. & Syph. **27**:851 (May) 1933.

LOUIS ADOLPHUS DUHRING

A GREAT AMERICAN DERMATOLOGIST

PAUL E. BECHET, M.D.
NEW YORK

"The importance of collecting and preserving facts in connection with whatsoever department of science, cannot be overestimated." These words form the opening sentence of Duhring's presidential address at the third annual meeting of the American Dermatological Association held on Aug. 26, 1879. Duhring practiced what he preached. In the Department of Dermatology at the University of Pennsylvania, under the reverent guardianship of Fred D. Weidman and Robert L. Gilman, there is a dilapidated old trunk filled to the brim with notes on almost every conceivable dermatologic subject, in the handwriting of Duhring. His devotion to dermatology breathes from every written word, and the patience, industry and effort represented by this store of notes are eloquent testimony to the high intellectual plane on which he lived.

THE MAN

Duhring was born in Philadelphia on Dec. 23, 1845. His father, Henry Duhring, and his mother, Caroline, were well to do and had social prominence. Duhring's childhood was spent in an agreeable environment, in the city home at 259 North Sixth Street and in the nearby country mansion at Bala, overlooking the Schuylkill River. His was a musical family. Duhring himself was an accomplished musician and when resident physician at the Philadelphia (Blockley) Hospital, he organized the Blockley brass sextette with Roland G. Curtin, J. Ewing Mears, Samuel S. Stryker, Isaac E. Roberts and A. W. C. Beecher as the other members. Later Arthur Van Harlingen took Mears' place. The band frequently entertained and delighted its audiences, composed of friends. They played also for the inmates of the insane department of the hospital and Dr. Van Harlingen and Dr. Stelwagon have both commented on the soothing effect of the music on the insane.

As a boy Duhring was of a retiring disposition, and showed little liking for athletics. He was a student and an avid reader. He was meticulous in his dress, and as he grew to manhood he developed a great fondness for society and social functions. During his student days at the University of Pennsylvania he met Arthur Van Harlingen. They were interns together at the Philadelphia Hospital, and a deep friendship and close association resulted, which lasted until Van Har-

lingen retired from the University of Pennsylvania and the foundation of the Philadelphia Polyclinic in 1885. They always remained close friends.

About the time that Duhring left Blockley, just before he departed for his studies abroad, his whole temperament underwent a change; whereas he had been cheerful, sociable and light-hearted, he became reserved and serious. Van Harlingen has stated "In after years I cannot recall any occasion when I have seen him smile or heard him laugh. His absorption in his work was absolute and complete." On the other

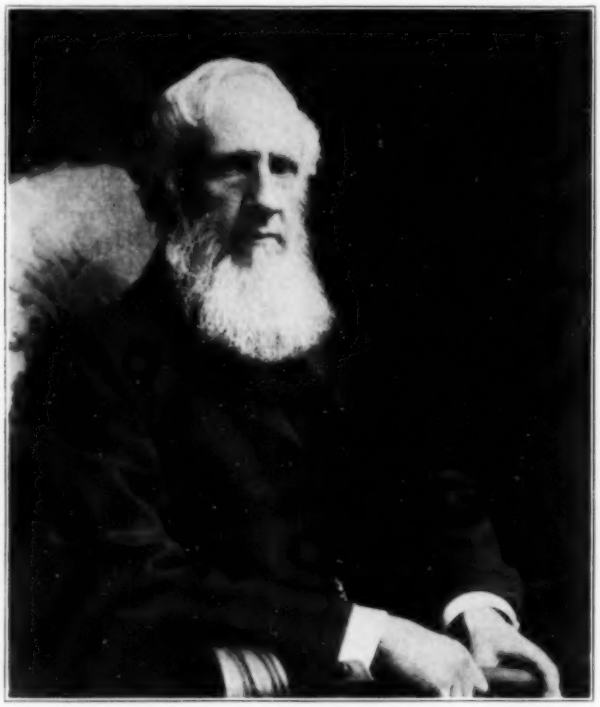

Fig. 1.—Louis Adolphus Duhring, 1845-1913.

hand, Stelwagon has noted that despite his austerity he always remained a delightful dinner guest, and showed an extraordinary amount of courtesy and deference to his hostesses, a trait which greatly endeared him to them, and made his visits most welcome. Others testify to the same charm of manner in social gatherings. It is said that this change in personality occurred shortly after the death of a young lady of whom Duhring was very fond, who was looked on as his fiancée. He apparently never completely recovered from the shock, for from that time on he led a more and more secluded existence, and seemed entirely engrossed in his work.

In 1892 he suffered further grief in the death of his sister, Julia, to whom he was so deeply devoted that in his will, many years later, he stated: "I order and direct that my executors shall have my remains interred alongside my sister Julia."

In later life Duhring was much alone. He had practically no intimates. At meetings he took part only in those discussions that touched on travel, books and the abstruse problems of dermatology.

About 1885 there developed symptoms of neurasthenia which culminated with a serious nervous breakdown. He was absent for long periods from the office and the university. He was fortunate at this time to have as a successor to Van Harlingen, Henry W. Stelwagon, first as his assistant at the university and later as an associate in his office. Stelwagon remained with him until 1890, when Duhring recovered sufficiently to resume full charge of his office and university duties. Subsequently Milton B. Hartzell succeeded Stelwagon.

Duhring's judgment of men and his recognition of merit were well exemplified by his choice of assistants. Van Harlingen, Stelwagon and Hartzell by their brilliant work were a credit to their great preceptor. Duhring, though much improved in health, was never well entirely; he was constantly combating illness. The symptoms were many and vague, and consisted chiefly of cardiac irritability and an ill-defined abdominal uneasiness which persisted until his death.

In 1910 he resigned as professor at the University of Pennsylvania, retired from active practice, and thereafter devoted himself, with great success, to the management of his estate. Duhring died on May 8, 1913.

The autopsy showed a constricting band over the ileum, which seemed, directly or indirectly, to be the cause of his death. In death as in life he showed his devotion to the advancement of medicine and the alleviation of suffering: He left his estate of more than $1,250,000 chiefly to the medical department of the University of Pennsylvania and the College of Physicians.

HIS PROFESSIONAL CAREER

Duhring's education began in private schools in Philadelphia. He entered the college department of the University of Pennsylvania in 1861 and remained until the end of his junior year in 1863. In July 1863, he enlisted in the Thirty-second Regiment, Pennsylvania Volunteers, and was honorably discharged in October of the same year. He then entered the medical department of the University of Pennsylvania, graduating March 14, 1867. The subject of his graduation thesis was "Nervous Gout." He immediately entered the Philadelphia (Blockley) Hospital, where he served as resident physician for fifteen months. His interest in dermatology was aroused at Blockley where he had under his

care an old man with a painful neuroma of the skin. He began to examine patients carefully for cutaneous diseases both in the hospital and in the outpatient department. At that time little if any interest existed in diseases of the skin as a specialty. Duhring's interest and enthusiasm soon attracted the attention of the hospital authorities, who granted him for his special work the use of a room for examination and dispensary purposes, which soon became known by his colleagues as the "diseases of the skin ward."

His internship over, Duhring left for Europe in July 1868, to seek special training in dermatology. In the General Hospital of Vienna, he

Fig. 2.—The Blockley Band, 1867.

joined the celebrated school of Hebra, and by his brilliant work attracted the attention of that master teacher, and became his personal companion on his dermatologic rounds. He later enjoyed the friendship of most of the leading dermatologists of Berlin, Paris and London, where he learned the methods of each. He studied oriental diseases of the skin in Constantinople, and leprosy in Norway. He worked every day of his two years in Europe without vacation and his joy in the work is reflected in his letters to the *Philadelphia Medical Times,* one each from Vienna, Paris and London. On his return to the United States he visited various centers, and made the acquaintance of the few dermatologists then in practice.

Duhring began to practice dermatology in Philadelphia in 1870. He organized the Dispensary for Skin Diseases at 216 South Eleventh Street, with Arthur Van Harlingen as his assistant, and he remained in active charge until 1880, when he was succeeded by Stelwagon. In 1871 Duhring was appointed lecturer on diseases of the skin at the University of Pennsylvania, the start of a teaching career that was to last some forty years. So successful were his methods as a teacher that his lecture-room was always crowded, despite the fact that attendance at the time was not compulsory. His friend and associate, Van Harlingen, was also his assistant at the university until 1885. In 1876 he became clinical professor of dermatology and in 1890 full professor. He resigned in 1910 to become professor emeritus and honorary curator of the Dermatologic Museum. In June 1912, the university conferred on him the degree of Doctor of Laws.

In 1876 a department for diseases of the skin was opened at the Philadelphia (Blockley) Hospital, and Duhring was made the visiting dermatologist, where he continued in sole charge until 1887, when, at his suggestion, Stelwagon shared the service.

Duhring was most active in organizing the American Dermatological Association, both at the preliminary meeting held in the rooms of the Section of Practical Medicine at the meeting of the American Medical Association in Philadelphia on June 7, 1876, and at the International Medical Congress in September 1876, when the association was founded. He was its first vice president, and twice president.

Duhring's ability gained for him as great a reputation abroad as at home, and he was made an honorary or associate member of dermatologic societies in London, Paris, Berlin and Vienna.

HIS WORK

In 1870, at the age of 25, he started with Dr. F. F. Maury *The Photographic Review of Medicine and Surgery*, a monthly journal which continued for two years. In its twenty-four numbers there were photographically represented forty-eight rare and interesting cases. Among its contributors were such well known men as S. Weir Mitchell, Joseph Pancoast, Samuel D. Gross, W. W. Keen, Arthur Van Harlingen and Thomas G. Morton.

Duhring's first contribution to dermatologic literature was a paper on "The Pathology of Alopecia Areata" which was published in the *American Journal of the Medical Sciences* in July 1870, and his last was "Treatment of Certain Chronic Inflammatory Skin Diseases," in the *Journal of Cutaneous Diseases*, 1909. In all he contributed to dermatologic literature approximately seventy-eight articles. Between 1884 and

1891, he wrote his famous series of papers, about eighteen in all, on dermatitis herpetiformis (Duhring's disease), an invaluable service, for it clarified a disease which had hitherto been described under such a mixed symptomatology and nomenclature that it was confusing. The papers were so clear and concise that they overcame the arguments of the opposition, led by Kaposi, and the disease has long since been established as a clinical entity.

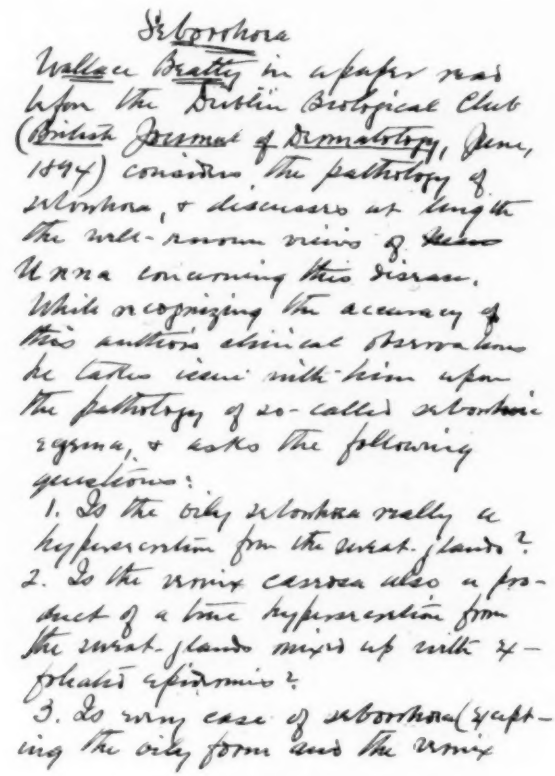

Fig. 3.—Autograph manuscript.

The first part of his "Atlas" appeared in 1876, and the subsequent eight parts were published at intervals of from six to eight months. The entire work contained thirty-six chromolithographic plates by the artist Faber. They represented the more familiar cutaneous diseases, Duhring wisely refraining from depicting the rarer dermatoses, as the work was intended for the general practitioner. The enterprise was costly, and it was in large part financed by Duhring. In 1877 his "Practical Treatise on Skin Diseases" was published by J. B. Lippincott and Company, dedicated to his old master Ferdinand Hebra. The book

PART II.

[2-line Pearl lightface No. 2.]

SPECIAL DISEASES.

[2-line Minion lightface No. 4.]

CLASS I.

[Pica old style extended.]

ANOMALIÆ SECRETIONIS—DISORDERS OF SECRETION.

[Pica No. 11 capitals.]

SEBORRHŒA.

[Long Primer old style antique capitals.]

..., Pityriasis; Stearrhœa; Steatorrhœa; Fluxus Sebaceus; Cutis Unctuosa; ... Saceæ; Seborrhagia; Tineæ Furfuraceæ; Tineæ Amaintaceæ; Tineæ Asbes... Ichthyosis Sebaceæ; Dandruff; Dandrif; *Germ.*, Schmeerfluss; Gneis; *Fr.*, ...Sebacée.

[Brevier No. 7.]

SEBORRHŒA IS A DISEASE OF THE SEBACEOUS GLANDS CHARACTERIZED ...AN EXCESSIVE AND ABNORMAL SECRETION OF SEBACEOUS MATTER, FORM... UPON THE SKIN AN OILY COATING, CRUSTS, OR SCALES.

[Long Primer No. 8 small capitals.]

Symptoms.—Seborrhœa may appear on any portion of the body,

...ier antique No. 5
... Small Pica body.]

...ugh, like the majority of cutaneous affections, it has favorite localities

[Small Pica No. 10.]

Fig. 4.—Proof sheet of the title page of part 2 of "Cutaneous Medicine."

was carefully prepared. Its text is clear and simple, its diction scholarly and the definition and exposition of the varied dermatoses comprehensive and presented in a remarkably interesting manner. With this book, Duhring established himself as a leader in dermatology. The work was enthusiastically received. It went through three editions, and was translated into French, Italian and Russian, a rare and almost unheard of honor for an American, at that time. Duhring then had scarcely reached the age of 32. The second edition, published in 1877, contained a number of illustrations, reproductions from pen and ink drawings by Van Harlingen.

Twenty years later, despite failing health, Duhring undertook the preparation of an encyclopedic work, which was to be published in parts, entitled "Cutaneous Medicine." The first number appeared in 1895, and the second in 1898. These two parts were profusely illustrated and the references carefully tabulated. They represented an enormous labor and were enthusiastically welcomed by the medical world. All the material accumulated for the third part was destroyed by fire. This disheartening blow, plus his poor health, proved insuperable, and the work was never completed. A chapter on cutaneous diseases in collaboration with Stelwagon appeared in Pepper's "System of Medicine."

I wish to acknowledge my indebtedness to two men, who knew Duhring well and admired him no less than I did: Dr. Van Harlingen, who furnished me with twelve pages of biographic data in his own hand, and Dr. Stelwagon, whose "Memoir on Duhring" published in the *Transactions of the College of Physicians of Philadelphia* in 1914 far outshines my humble effort to record the career of this great man. Mrs. Stelwagon also was of great help in the preparation of this account.

CUTANEOUS RHEUMATIC NODULES

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A careful review of the literature on rheumatism fails to disclose any definite description of cutaneous rheumatic nodules. The reports thus far have been limited to a description of subcutaneous rheumatic nodules. The clinical reports are more numerous than the pathologic, and most of them present no pathologic description. The nodules are called subcutaneous, but the number of these which may have been cutaneous is not known, for there is no description of biopsies. Since the cases presented here showed rheumatic nodules in the cutis, it is of interest to report them. Another interesting feature is that they occurred in adults. The earliest cases of subcutaneous rheumatic nodules were seen in children and were reported by Hillier [1] in 1868. Meynet,[2] in 1875, described a case in a boy of 14 years, who had several attacks of acute articular rheumatism with freely movable ephemeral soft nodules along the tendons near the joints of the fingers, wrists, elbows and knees and also along the vertebral column, on the forehead and in the parietal and occipital regions. Barlow and Warner,[3] in 1881, described twenty-seven cases occurring in children and adolescents, the oldest being 18 years of age.

In 1920, Brennemann [4] reported a number of cases occurring in children. He described the nodules as being deep-seated, always in connection with the deep fascia, tendons or periosteum. The lesions do not appear in the ordinary case of chorea or rheumatism without cardiac complication, but rarely they appear before the heart is affected in severe cases of endocarditis. In these cases the appearance of a new crop of nodules prognosticates a renewed serious invasion.

The first description of subcutaneous rheumatic nodules in an adult was given by Troiser and Brocq [5] in 1881. The patient, a man of 45 years, during the decline of an attack of acute articular rheumatism

From the Department of Dermatology, Northwestern University.

1. Hillier, Thomas: Diseases of Children, Philadelphia, 1868; cited by Jackie, E.: Frankfurt. Ztschr. f. Path. **22**:82, 1919.

2. Meynet, P.: Rheumatisme articulaire subaigu avec production de tumeurs multiples, Lyon méd. **19**:495, 1875.

3. Barlow, T., and Warner, F.: On Subcutaneous Nodules, Tr. Internat. M. Cong., London **4**:116, 1881.

4. Brennemann, J.: The Incidence and Significance of the Rheumatic Nodules in Children, Am. J. Dis. Child. **18**:179 (Sept.) 1919.

5. Troiser and Brocq: Rev. de méd., Paris **1**:297, 1881.

with mitral endocarditis and bilateral pleural effusion, had successive crops of subcutaneous nodules occurring on the occiput, forehead and ears. The nodules varied in size from that of a pea to that of a hazelnut; they were round or oblong, well defined, painful on firm pressure and freely movable beneath the skin. In 1891, Angel Money [6] differentiated between superficial and deep rheumatic nodules. He stated that the superficial lesions are more numerous, smaller, more closely aggregated, more painful and more transient than the deep lesions. He gave no histologic description, so that one does not know whether his so-called surface lesions were cutaneous or subcutaneous.

The first case reported in this country was from Osler's clinic in December 1888 by J. K. Mitchell.[7] He described a man of 42 years with multiple arthritis and numerous painless nodules over the joints of the fingers and knees varying in size from that of a pinhead to that of a grain of wheat. In 1895, Futcher,[8] also from Osler's clinic, reported nine cases of subcutaneous fibroid rheumatic nodules in patients varying in age from 13 to 60 years. He found that the nodules usually did not appear until after the acute symptoms had subsided and that rheumatic patients with endocardial complications seemed to be most liable to have subcutaneous fibroid nodules.

The first description of the histology of subcutaneous nodules was given by Hirschsprung [9] in 1881; he noted an increase in the number of blood vessels. In 1883, Cavafy [10] described proliferation of the intima of the blood vessels which sometimes obliterated the lumen. Futcher,[8] in 1895, stated that the nodules are made of fibrous tissue in varying stages of development with a marked increase in the number of blood vessels and a thickening of the intima; he also noted an infiltration with small round cells, fibroblasts, polymorphonuclear leukocytes and occasional giant cells. In addition to these observations, Frank [11] in 1912 and Clawson [12] in 1929 noted in the center of most of the nodules a homogeneous substance consisting of necrotic material and fibrin.

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6. Money, Angel: Surface and Subsurface Nodular Rheumatism, Lancet **1**: 540, 1891.

7. Mitchell, J. K.: Univ. M. Mag. **1**:161, 1888-1889.

8. Futcher, T. B.: A Study of Subcutaneous Fibroid Nodules, Bull. Johns Hopkins Hosp. **6**:133, 1895.

9. Hirschsprung, H.: Eine eigenthümliche Localization des Rheumatismus acutus im Kindesalter, Jahrb. f. Kinderh. **16**:324, 1880-1881; cited by Frank, P.: Berl. klin. Wchnschr. **49**:1358, 1912.

10. Cavafy: Rheumatic Nodules, Brit. M. J. **1**:622, 1883.

11. Frank, P.: Ueber den Rheumatismus nodosus mit besonderer Berücksitigung des pathologischanatomischen Befundes, Berl. klin. Wchnschr. **49**:1358, 1912.

12. Clawson, B. J., and Bell, E. T.: Valvular Diseases of the Heart, Am. J. Path. **2**:193, 1926.

REPORT OF CASES

Thus far the reports of cases and histologic descriptions refer to subcutaneous rheumatic nodules. To my knowledge the following two cases are the first to be reported of cutaneous rheumatic nodules:

CASE 1.—Mrs. A., 46 years old, was admitted to the medical department of Northwestern University on March 17, 1933. She complained of pain in the hands, wrists, knees and elbows, which began the previous July, and had been present since then with remissions and exacerbations. In January 1933, nodules appeared on the volar and dorsal surfaces of the fingers of both hands and on the palms. These nodules were not painful or tender except on firm pressure; they were red, ranged

Fig. 1.—Rheumatic nodules on the fingers.

in size from that of a pinhead to that of a hazelnut and lasted six weeks. A new crop appeared just prior to admission.

Physical examination revealed a white woman about 50 years of age, not actually ill. The essential findings were swellings and extreme tenderness of the interphalangeal and metacarpophalangeal and carpal joints with a glazed appearance of the overlying skin and pain on motion. She was unable to close her hands. The knees and elbows were likewise swollen and tender with pain and crackling on movement. All her teeth had been extracted. The tonsils were ragged, hypertrophied and showed large irregular crypts. The heart and lungs were normal. The blood pressure was 110 systolic and 70 diastolic. The basal metabolic rate was minus 2 per cent. The sedimentation index, by the modified Westergren method, was 32.5 per cent, the normal value being from 1 to 7 per cent. The urine was normal. The blood showed secondary anemia: hemoglobin, 77.2 per cent; red cells,

3,840,000; white cells, 7,000; lymphocytes, 18 per cent; large mononuclears, 6 per cent; polymorphonuclear leukocytes, 75 per cent, and eosinophils, 1 per cent. A roentgenogram of the wrists and hands showed slight decalcification of the bones and some swelling of the soft tissue but no proliferative or destructive changes in the joints.

On May 8 she was transferred to the dermatologic department presenting nodules on the volar and extensor surfaces of the fingers of both hands and on the palms. The nodules were superficial, varied in size from that of a pinhead to that of a hazelnut and were freely movable and sharply defined; the overlying skin was red and taut. The nodules were not painful, but the joints of the hands, wrists,

Fig. 2.—Rheumatic nodules on the face and neck with some excoriations caused by picking.

elbows and knees were painful. A specimen was taken from the left thumb for biopsy. These nodules lasted about a month and disappeared, leaving no trace.

A new crop appeared on June 19, with a similar distribution on the hands and, in addition, on the neck, forehead and cheeks. The lesions did not itch, but the patient repeatedly picked at them. They disappeared by the end of July and did not recur. A second specimen for biopsy was taken from the middle finger.

Dr. R. H. Jaffé made the following histologic report on the biopsy specimen from the left thumb: The epidermis was slightly thickened and the layer of keratohyalin was well developed. Between the prickle cells were single cells which were swollen with clear cytoplasm and pyknotic nuclei. The papillary layer of the cutis appeared loosened; the lymph vessels were dilated, and the fibrocytes were swollen. There was slight acanthosis, and at the height of the

tips of the rete pegs the cutis showed loose accumulations of small round cells, histiocytes and occasional plasma cells which centered about capillaries with swollen endothelial cells.

In the reticular layer of the cutis the edema and the perivascular infiltration were more marked, and the connective tissue trabeculae were often separated by rows of round cells which radiated from the cellular adventitia of the capillaries and the precapillary and postcapillary blood vessels. These vessels showed a slight

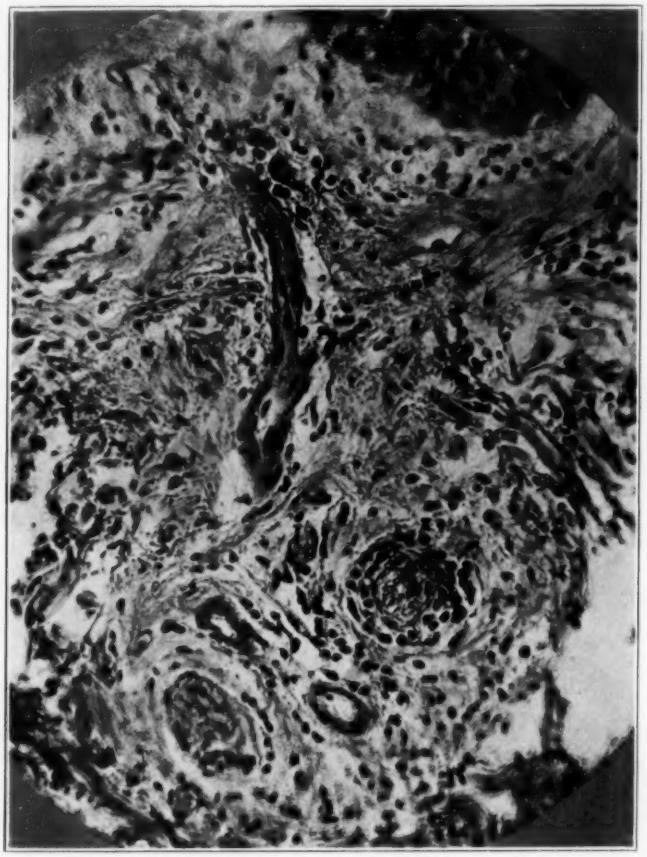

Fig. 3.—Diffuse infiltration by round cells, histiocytes and occasional plasma cells in the reticular layer of the cutis.

thickening of the wall caused by a swelling and increase in the number of endothelial cells. The adventitial cells, too, were swollen and more numerous than normal. About the sweat glands were similar infiltrations which, however, were less marked than those about the blood vessels. In the subcutaneous fat tissue corresponding to the center of the infiltrated area was a small artery, the endothelial cells of which were so much swollen that they resembled the epithelial lining of a gland. Sheets of desquamated endothelial cells with fibrin, leukocytes and round cells filled the lumen. The media stained pale; the muscle fibers were poorly differentiated, and the nuclei were shrunken; the adventitia contained

round cells and leukocytes, and similar cells were found between the adjacent fat cells. The small cutaneous nerves were surrounded by several rows of lymphocytes.

CASE 2.[13]—A youth of 15 years of age was admitted to the Cook County Hospital, complaining of pain in the joints of three weeks' duration. Two days prior to the onset of the arthritic pains a crop of small red "pimples" had appeared on the extremities and chest. The joints involved were the right knee, right elbow, right shoulder and left wrist; they were warm, tender and painful on motion. The acute symptoms lasted one day in each joint and then involved another joint. The

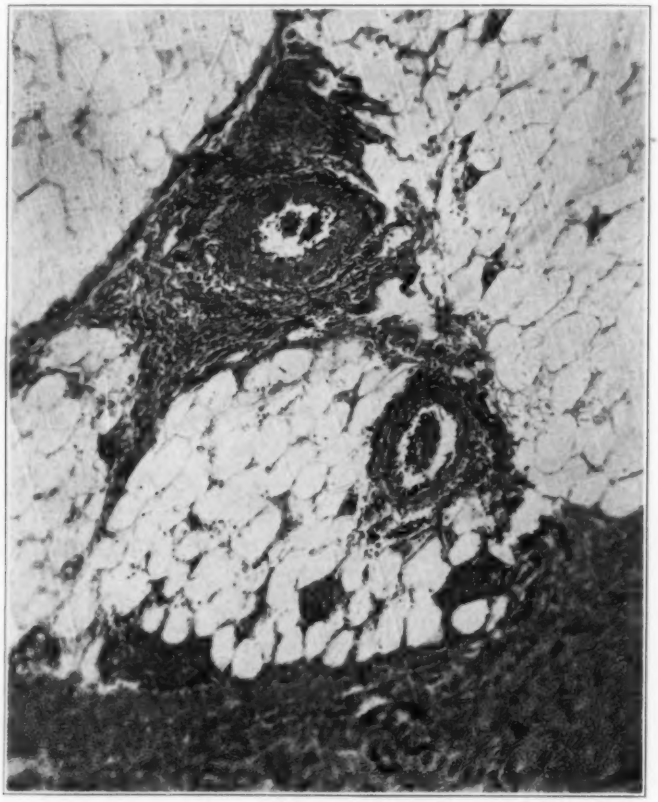

Fig. 4.—Proliferation of the endothelial cells of an arteriole with degeneration of the media in the areolar tissue.

attack was attended by fever and transient sore throat. Some of the "pimples" had disappeared, but a number persisted. On admission the temperature was 99.8 F., the pulse rate, 96, the respiratory rate, 26 and the blood pressure 100 systolic and 60 diastolic. There were small red papules over the arms, chest and legs. The throat was injected. The left border of the heart was substernal; there was a soft blowing systolic murmur at the apex. Repeated blood cultures were negative. The electrocardiogram showed sinus arrhythmia. The blood showed: hemoglobin, 65 per cent; red cells, 3,331,000; white cells, 13,400; poly-

13. Dr. Frank B. Lusk provided the history of this case.

morphonuclear neutrophils, 80 per cent; eosinophils, 1 per cent, and lymphocytes, 19 per cent. A roentgenogram of the chest showed a normal condition. Repeated urinalyses presented no abnormalities. For about five weeks he had a continuous elevation of temperature, which at times had a septic curve. During this time the acute arthritic disturbances passed from one joint to another, and he had several new crops of cutaneous lesions; some appeared on the dorsum of the right foot,

Fig. 5.—Slight thickening of the epidermis, with marked cornfication. Perivascular infiltration throughout the cutis.

some on the left leg and some on the right hand. The systolic murmur at the apex persisted, but the arthritic and cutaneous manifestations cleared up entirely, and he was discharged about ten weeks after admission.

Dr. R. H. Jaffé made the following histologic report: The epidermis showed marked cornification, but the keratohyaline layer was poorly differentiated. There were single balloon cells between the elements forming the prickle cell layer.

The basal layer contained a moderate amount of yellowish-brown pigment granules. Throughout the cutis the blood vessels were prominent because of thick cellular coats composed of polymorphonuclear leukocytes, eosinophilic leukocytes and small round cells. The infiltrations extended into the wall of the vessels, obscuring the differentiation of the layers. The lumen was often filled by proliferated and desquamated endothelial cells, leukocytes and mononuclear cells, between which a few erythrocytes were found.

DIFFERENTIAL DIAGNOSIS

1. Erythema nodosum occurs chiefly on the anterior surface of the legs and rarely on the face or fingers. The lesions are bright red, shiny and tender; they rarely recur.

2. In nodular syphilis the lesions are less numerous, more indolent in their course and often unilateral, and they tend to break down and ulcerate. They are not associated with pains in the joints.

3. Heberden's nodes are small bony outgrowths at the terminal phalangeal joints, which develop gradually and persist.

4. Erythema elevatum diutinum is frequently associated with rheumatism. The lesions consist of nodes and infiltrated plaques which are freely movable in the skin and have a tendency to recur. Histologically, however, the lesions consist of infiltrates made up chiefly of polymorphonuclear leukocytes.

5. Subcutaneous rheumatic nodules occur frequently in children in connection with endocarditis and severe types of rheumatism. The nodules are deep-seated, always in connection with the deep fascia, tendons or periosteum. They are not freely movable, and the skin over them appears normal.

6. Bromides and iodides may produce nodular lesions; they may be ruled out by the history, by their irregular distribution, by the comparatively extensive subcutaneous lesions with little systemic disturbance, by finding the drug in the urine, by the clearing of the lesions after medication is stopped and by their recurrence on resuming medication.

SUMMARY

1. A brief review of the literature on subcutaneous rheumatic nodules is given.

2. Two cases of cutaneous rheumatic nodules occurring in adults, with biopsies, are presented.

THE FUNGI OF BLASTOMYCOSIS AND COCCIDIOIDAL GRANULOMA

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The term "blastomycosis" is often applied to any disease in the lesions of which the causative fungus appears as rounded cells more or less resembling those of yeast. Consequently this designation has been used for different mycoses which have little clinical or pathologic similarity and which are caused by unrelated species of fungi. On the other hand, different names are applied by different clinicians to what are evidently infections by the same fungus. The terminology of the fungi concerned is even more chaotic.

The first step necessary toward clearing this confusion and obtaining an orderly understanding of these infections appears to be a careful study of the causative fungi and the establishment of criteria by which distinct types may be recognized.

The present report is based on a study of fungi from three important types of mycotic infection.

TYPE I: CRYPTOCOCCUS HOMINIS (BUSSE AND BUSCHKE 1894) (VUILLEMIN, 1901)

Cryptococcosis.—In 1894 Busse [1] and Buschke [2] reported a fatal infection in a woman who at first presented a large abscess of the tibia filled with gelatinous fluid, and in whom other osseous and visceral lesions of similar character and cutaneous ulcerations developed subsequently. In the various lesions during the patient's life or post mortem Busse and Buschke observed a yeastlike fungus which was capsulated, both in tissue and in culture. With cultures of this fungus they produced similar lesions in mice and also in the patient by reinoculation. They noted certain pathologic features which seem characteristic of this particular mycosis: the mucinous character of the exudate, the fact that apparent abscesses were made up of masses of yeast cells containing few definite leukocytes and the lack of inflammatory reaction about many of these collections of parasites; this was especially striking in the brain of inoculated mice.

From the Laboratory for Medical Mycology, College of Physicians and Surgeons, Columbia University.

1. Busse, O.: Centralbl. f. Bakt. (Abt. 1) **16**:175, 1894; Virchows Arch. f. path. Anat. **140**:23, 1895.

2. Buschke, A.: Deutsche med. Wchnschr. 1895, W. Vereins Beilage, p. 14.

Busse and Buschke referred to the disease as "saccharomycosis" or simply "yeast infection" and Buschke [3] later called it "blastomycosis" or, to distinguish it from Gilchrist's disease, "European blastomycosis."

Cases have since been reported under the name of blastomycosis from Europe, America and Australia by Versé,[4] Brewer and Wood,[5] Williams,[6] Gáspár [7] and others; these cases, if one may judge from the description of the lesions and of the fungi recovered, were of the same type as that of Busse and Buschke. This similarity and the distinction from Gilchrist's disease are, however, seldom stated in the reports.

The Fungus.—The strain studied was obtained from the American Type Culture Collection at Chicago and was labeled as follows: "Cryptococcus hominis (Busse) Vuill. No. 4189 Centraal.-Bur. v. Schimmelcultures, Baarn, Holland."

Morphologic Characteristics. — In Lesions: In fresh sodium hydroxide preparations from the tissues of inoculated rats the organism appears as rounded or slightly oval budding cells of varying size but averaging about 8 microns in diameter. The buds have thinner walls than the mother cell. The walls of the larger cells may be highly refractive. Surrounding the cells is a clear area equal to or twice the diameter of the cell; this is the so-called capsular substance. This substance may surround the individual cells, or groups of cells may appear in this clear area like globules in a gelatinous mass. Numerous granules may be seen within the cell; many of these granules are fat, as may be shown by staining with sudan III. In a mounting fluid composed of sudan III and glycerin the appearance is even more striking (fig. 3). The wall is greenish; the granules of fat, pink, and the clear capsular zone, pronounced. Sometimes concentric rings appear in the capsular substance.

In sections the cells stain irregularly, but a thick wall is usually visible. The capsular substance is usually unstained. Some cells are surrounded by a thick layer of eosin-staining substance within which buds may lie. Outside of this there is a wide unstained area (fig. 10).

In Culture: In cultures on various mediums only similar rounded cells varying in size but usually 5 or 6 microns in diameter are seen (fig. 2*A*). These cells reproduce by budding. Sometimes chains of three or four cells may be found. There is no mycelium. In old cultures of a month or more which have begun to dry, large, thick-walled

3. Buschke, A., in Born, G., and Flügge, K.: Bibliotheca medica, Cassell, T. G. Fischer, 1902, Pt. D,[II] Dermatologie und Syphilidologie, no. 10.

4. Versé, M.: Verhandl. d. Deutsch. path. Gesellsch. **17**:275, 1914.

5. Brewer, G. E., and Wood, F. C.: Ann. Surg. **48**:889, 1908.

6. Williams, J. R.: M. J. Australia **2**:185, 1922.

7. Gáspár, I.: Blastomycotic Meningo-Encephalitis: Report of a Case, Arch. Neurol. & Psychiat. **22**:475 (Sept.) 1929.

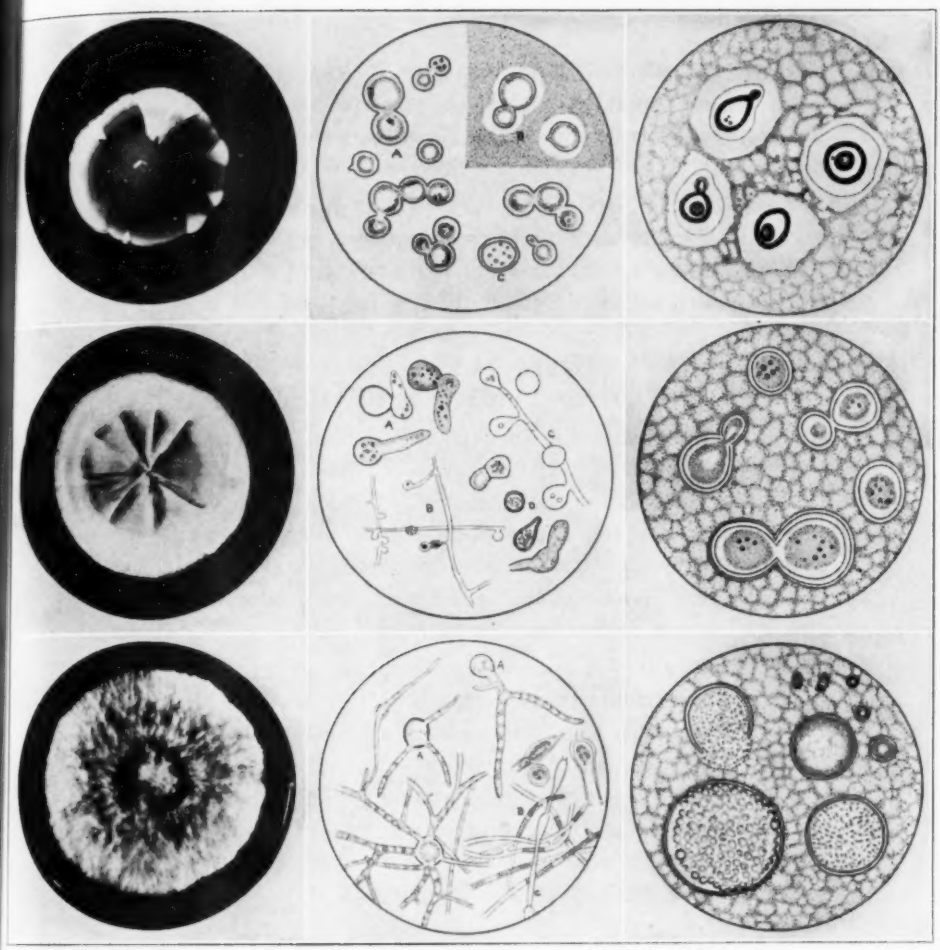

Fig. 1 (C. hominis [Vuillemin]).—Moist, smooth, cream to tan colony.

Fig. 2 (C. hominis [Vuillemin]).—*A*, budding cells from agar culture; *B*, capsule as seen in india ink mount; *C*, thick-walled cell; reduced from × 840.

Fig. 3 (C. hominis [Vuillemin]).—Cells from an inoculated rat; thick-walled budding cells surrounded by a capsule; reduced from × 840.

Fig. 4 (B. dermatitidis [Gilchrist and Stokes]).—White to cream, or light buff to tan, downy or fluffy colony.

Fig. 5 (B. dermatitidis [Gilchrist and Stokes]).—*A*, cells from tissue from forty-eight hour broth culture; reduced from × 420; *B*, mycelium and conidia from agar culture; reduced from × 280; *C*, same, reduced from × 800; *D*, thick-walled cells from old cultures; reduced from × 420.

Fig. 6 (B. dermatitidis [Gilchrist and Stokes]).—Budding cells from an inoculated guinea-pig; no capsule; reduced from × 840.

Fig. 7 (C. immitis [Rixford and Gilchrist]).—Grayish-white fluffy colony.

Fig. 8 (C. immitis [Rixford and Gilchrist]).—*A*, cells from tissue germinating in culture; *B*, mycelium and chlamydospore formation; *C*, racquet mycelium, reduced from × 420.

Fig. 9 (C. immitis [Rixford and Gilchrist]).—Thick-walled spherical cells from an inoculated guinea-pig; endospore formation; reduced from × 280.

nonbudding cells filled with granules may be seen (fig. 2 *C*). No ascospores have been found. A capsule develops in cultures as in tissue and may be best demonstrated in an india ink mount as suggested by Weidman (fig. 2 *B*).

Cultural Characteristics.—On various agar mediums containing sugar the organism appears as a moist cream-colored growth which with age may become yellow or darker. On maltose agar the giant colony, the surface of which remains smooth and moist, assumes a deep brown pigment (fig. 1). The mucoid consistency of the growth is a striking characteristic. There is no gaseous fermentation of any sugars. Gelatin shows only slight liquefaction after from six to eight weeks.

Pathogenicity.—Although this strain had been on artificial mediums for nearly forty years, it could be recovered from rats two weeks after intraperitoneal inoculation, and after a few such passages it produced gelatinous nodules in the omentum, spleen or lung, sometimes forming huge confluent masses. Busse stated that mice are the most susceptible animals and that lesions could occasionally be produced in dogs and guinea-pigs but not in rabbits.

Serum Reactions.—A specific agglutinating serum can be prepared by injecting into rabbits massive doses of this fungus. Such serums give distinct precipitin reactions with saline washings of agar cultures which presumably contain the capsular substance.

The strain here described corresponded well to the original descriptions of Busse and Buschke except in one respect. Busse [8] stated that his strain fermented dextrose with the production of gas, but later observers seem agreed as to the inability of this fungus to produce fermentation.

TORULA HISTOLYTICA

In 1905 von Hansemann [9] described a case of infection of the brain and meninges due to yeast. He did not refer to the work of Busse and Buschke although his fungus evidently resembled theirs. In 1916 Stoddard and Cutler [10] reported two cases of meningeal infection and named the fungus Torula histolytica. They believed it to be distinct from Cryptococcus hominis solely because Buschke [11] once stated that the latter formed spores (presumably ascospores)—a statement which he later retracted.[12]

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8. Busse, O.: Die Hefen als Krankheitserreger, Berlin, A. Hirschwald, 1897.

9. von Hansemann, D.: Verhandl. d. deutsch. Path. Gesellsch. **9**:21, 1905.

10. Stoddard, J. L., and Cutler, E. C.: Torula Infection in Man, New York, Rockefeller Institute for Medical Research, 1916, Monograph 6.

11. Buschke, A., in Kolle, W.; Kraus, R., and Uhlenhuth, P.: Handbuch der pathogenen Mikro-Organismen, ed. 2, Jena, Gustav Fischer, 1913.

12. Buschke, A., and Harry, F.: Dermat. Wchnschr. **76**:357, 1923.

In this way, however, a series of cases was described under the name of torula infection or torula meningitis although these cases were apparently due to the species of fungus described by Busse and Buschke. In some the lesions were found only in the central nervous system; in others they occurred in the bones, viscera and subcutaneous tissues as well. The mucinous character of the exudate and the scant reaction about collections of parasites previously noted by Busse are described as occurring in most of the lesions.

A strain labeled T. histolytica no. 2526 was obtained from the American Type Culture Collection. This strain was isolated from a case of meningitis reported by Freeman and Weidman.[13] A similar strain was obtained from the case of Shapiro and Neal.[14] In culture both of these strains proved indistinguishable from the Busse-Buschke strain in cultural characteristics and in morphology. The strain from the case of Freeman and Weidman showed the same capsulated cells in the tissue of inoculated rats. An antiserum was prepared against this strain. There was cross-precipitation between this and the Busse-Buschke strain, with complete reciprocal absorption of precipitins. These specimens of the so-called T. histolytica were evidently of the same species as the Cryptococcus hominis of Busse and Buschke. One can be certain only as to strains which one has studied at first hand, but the published descriptions furnish no valid grounds for doubting that the majority of fungi described under these two names are of one species.

Saccharomyces tumefaciens of Curtis,[15] however, shows minor differences and may be a separate but related species.

CRYPTOCOCCI FROM NORMAL SKIN

In a study of yeastlike fungi from normal skin[16] strains of capsulated cryptococci were encountered which by their form, cultural characteristics or agglutination reactions could not be distinguished from Cryptococcus hominis. The only distinction found was in pathogenicity. When injected intraperitoneally into rats the strains from normal skin could not be recovered after four or five days. It seems probable that they are avirulent strains of the same species.

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13. Freeman, W., and Weidman, F. D.: Cystic Blastomycosis of the Cerebral Gray Matter Caused by Torula Histolytica, Stoddard and Cutler, Arch. Neurol. & Psychiat. **9**:589 (May) 1923.

14. Shapiro, L. L., and Neal, J. B.: Torula Meningitis, Arch. Neurol. & Psychiat. **13**:174 (Feb.) 1925.

15. Curtis, F.: Presse méd. **3**:370, 1895.

16. Benham, R. W., and Hopkins, A. McH.: Yeastlike Fungi Found on the Skin and in the Intestines of Normal Subjects: A Survey of One Hundred Persons, Arch. Dermat. & Syph. **28**:532 (Oct.) 1933; The Cryptococci: Their Identification by Morphology and by Serological Reactions, to be published.

TERMINOLOGY

The question of the proper terminology for fungi of this type will be discussed elsewhere.[17] It seems best, however, in view of present knowledge, to retain for this organism the name given by Vuillemin [18]—Cryptococcus hominis. The T. histolytica of Stoddard and Cutler would then become Cryptococcus hominis. Since the generic term Cryptococcus (Kützing) em Vuillemin is commonly applied by medical mycologists to fungi imperfecti which appear only as round or oval cells that reproduce by budding, the diseases caused by these rudimentary fungi might be grouped under the cryptococcoses. The use of this term for the so-called European blastomycosis might help to lessen the confusion now existing. Buschke and Joseph [19] have emphasized the difference between European blastomycosis and Gilchrist's American blastomycosis (to be described subsequently), but many writers have failed to make any such distinction.

TYPE II: BLASTOMYCES DERMATITIDIS (GILCHRIST AND STOKES, 1898)

The organism described by Gilchrist and Stokes [20] as the cause of American blastomycosis is a hyphomycete quite distinct from the Cryptococcus of Busse and Buschke, and in general the disease seems distinguishable by its pathologic picture.

Blastomycosis.—In 1894 at a meeting of the American Dermatological Association Gilchrist described the case of a man with a lesion on the hand resembling a verrucous tuberculosis. In sections he found round and oval refractive bodies with thick walls from 10 to 23 microns in diameter which he believed to be vegetable parasites. Two years later he [21] reported this case in detail. In the same year in association with Stokes he observed a similar case with multiple lesions which contained the same type of organism. From miliary abscesses in these lesions he obtained in pure culture a fungus which developed a mycelium. He first described this fungus as a Oidium, but later he called the organism Blastomyces dermatitidis, and the disease which it caused, blastomycetic dermatitis.[22] Since then apparently similar cases have been described in various parts of the world, but it is impossible to make certain from the published descriptions in just which cases the fungi concerned were the blastomyces of Gilchrist. The largest number

17. Benham, R. W.: The Terminology of the Cryptococci with a Note on Cryptococcus Mollis (Kützing) 1833, to be published.

18. Vuillemin, P.: Rev. gén. de sc. pures et appli. **12**:732, 1901.

19. Buschke, A., and Joseph, A., in Jadassohn, J.: Handbuch der Haut und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 11, p. 825.

20. Gilchrist, T. C., and Stokes, W. R.: Bull. Johns Hopkins Hosp. **7**:129, 1896.

21. Gilchrist, T. C.: Johns Hopkins Hosp. Rep. **1**:269, 1896.

22. Gilchrist, T. C., and Stokes, W. R.: J. Exper. Med. **3**:53, 1898.

of cases have been reported from Chicago. The disease occurs in two forms, cutaneous and systemic. The cutaneous form apparently results from cutaneous inoculation and usually begins as a small papulopustule on the hand, face or any other exposed site. New lesions appear in the neighborhood and fuse to form a plaque with a raised border which slopes sharply down to the normal skin. Miliary abscesses are usually visible near the margin. The central portion is covered with adherent

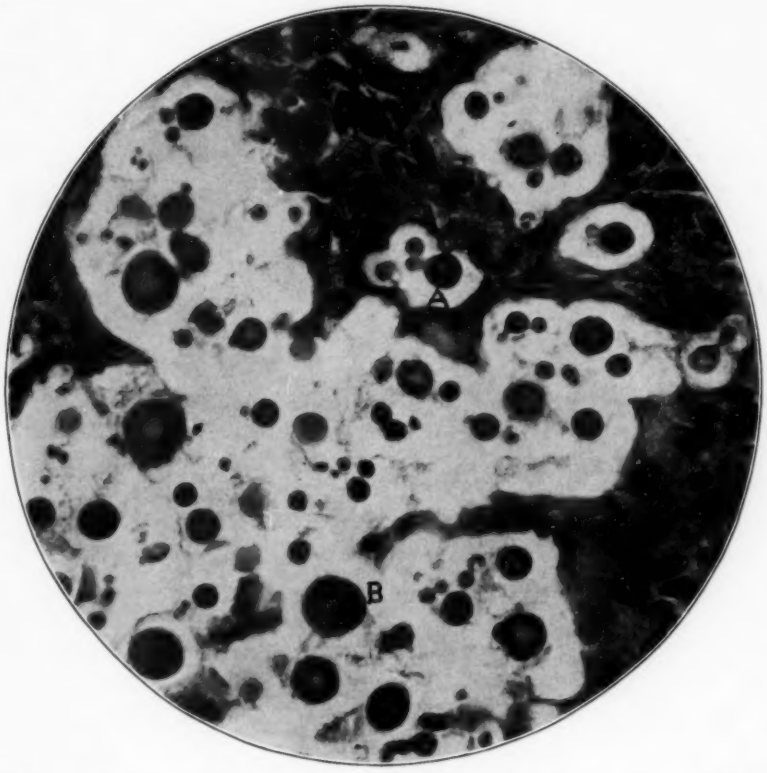

Fig. 10.—Section from the lung of a rat inoculated with Cryptococcus hominis. The cells are lying in a clear area, the capsular substance. *A*, thick-walled budding cell; *B*, cell surrounded by a dense layer of eosin-staining substance; × 500.

crusts which on removal expose a moist, deep red, papillomatous base. The disease may last for years, but it usually terminates in recovery.

The systemic form may follow a primary cutaneous infection which has extended to the lymph nodes, but more frequently it develops from a hidden focus which is probably in the lungs. Granulomatous lesions are found in the bones, viscera, meninges and subcutaneous tissues.

These lesions rupture and form chronic ulcers, or they may develop into verrucous lesions somewhat resembling the primary cutaneous form. Apparently these systemic cases of blastomycosis are difficult to differentiate clinically from cases of coccidioidal granuloma, and they have been confused with the cryptococcosis of Busse and Buschke. They are usually fatal but show some response to iodide therapy. This is often mentioned as a point differentiating them from coccidioidal granuloma.

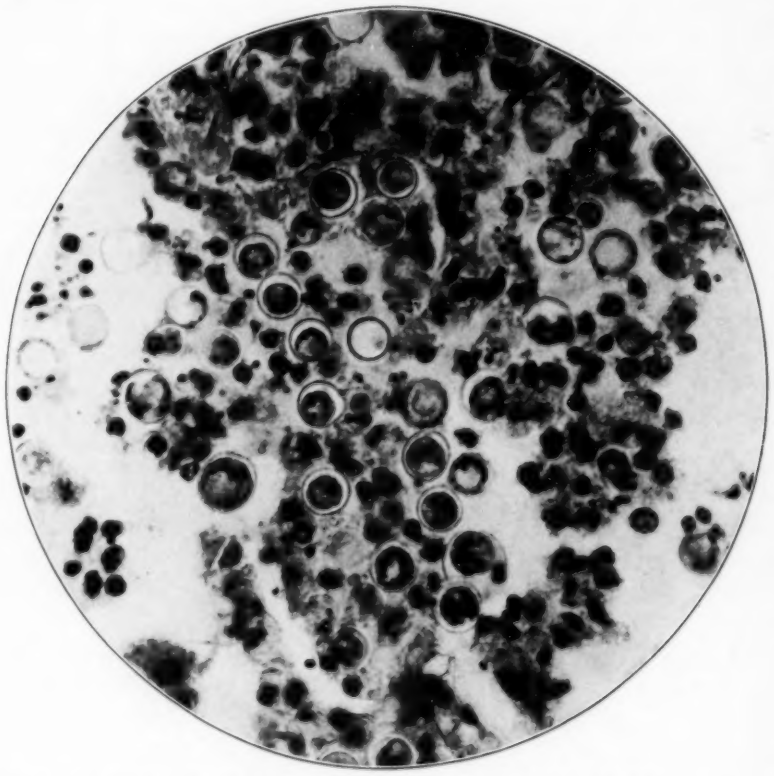

Fig. 11.—Section from the lung of a monkey inoculated with Blastomyces dermatitidis. Spherical budding cells showing a definite wall; × 500.

The Fungus.—The two strains described subsequently were isolated from cases of blastomycetic dermatitis similar to those first described by Gilchrist and Stokes (fig. 13). The cultures also answer well to the original descriptions by these authors.

Morphologic Characteristics.—In Lesions: In the patients' lesions and in those of inoculated animals the fungus cells are round or oval and usually from 8 to 10 microns in diameter, though some as large as 23 microns have been reported (figs. 6 and 11). They are larger and more uniformly round than the cells of Cryptococcus hominis. In

fresh mounts the wall is more refractive, and in sections it is more sharply differentiated from the granular cell contents. This wall is often referred to as a capsule, but there is no capsular substance comparable to that of Cryptococcus hominis. Buds of all sizes up to that of the parent cell are observed. The cells are usually highly granular. In fresh preparations this helps to distinguish them from globules of fat which may assume the form of budding cells and cause confusion.

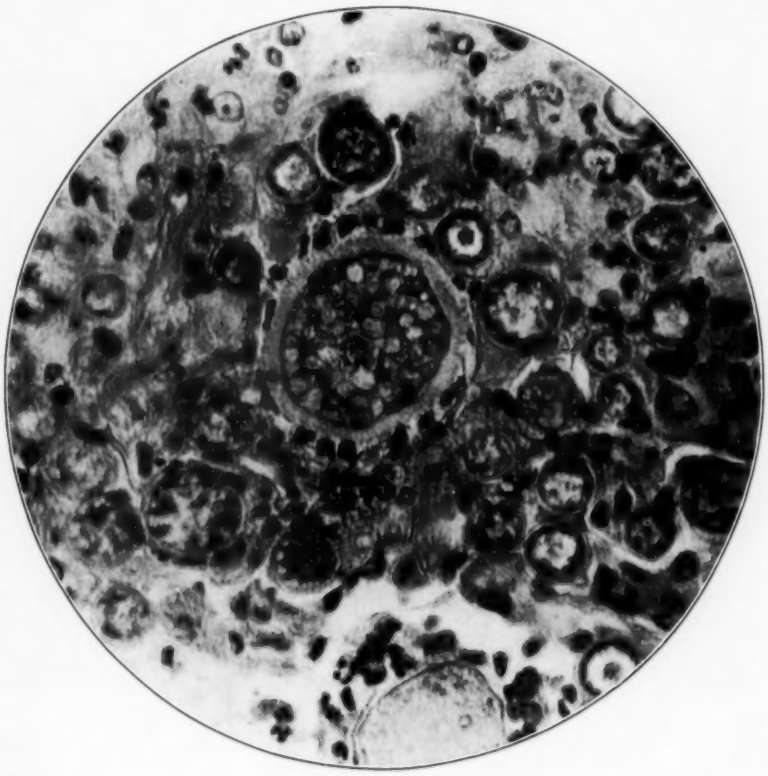

Fig. 12.—Section from subcutaneous tissue of a guinea-pig inoculated with Coccidioides immitis. Large spherical cell filled with spores, with the surface covered with spines; also younger cells; × 500.

In Culture: The structures most characteristic of this species seem to be conidia, which occur anywhere along the side of the hyphae or on the tips of short lateral branches (fig. 5 *B* and *C*). They appear first as knoblike projections which gradually enlarge. At first the wall is thin, and the contents are more or less homogeneous. Later the walls thicken, and the contents become more granular, giving somewhat the appearance of chlamydospores. These cells may become free and appear

to bud, resembling the cells observed in tissue. These conidia are found regularly in the downy or fluffy colonies to be described.

Stober,[23] Spring,[24] and Castellani,[25] as well as Gilchrist, noted these structures. Gilchrist and Stokes' original description (1896) of the organism reads:

> From the round or oval bodies there occurs a growth of numerous long, branching threads of mycelium, at first clear, later containing numerous fine granules or larger round refractive bodies. At various points along the sides of these hyphae numerous small knob-like projections of the limiting membrane occur which gradually enlarge and at last form large round cells or conidia. These either remain attached by means of narrow stems or sterigmata, or become free, and then greatly resemble the cells observed in the tissues and young colonies.

Fig. 13.—Case of blastomycosis from which one of the strains of Blastomyces dermatitidis studied in this laboratory was isolated.

Intercalary chlamydospores are found in great numbers in old cultures. Many of these appear to bud (fig. 5 *D*). Cells from a forty-eight hour broth culture show the beginning of mycelial growth (fig.

23. Stober, A. M.: Systemic Blastomycosis. A Report of Its Pathological, Bacteriological and Clinical Features, Arch. Int. Med. **13**:509 (April) 1914.

24. Spring, D.: Comparison of Seven Strains of Organisms Causing Blastomycosis in Man, J. Infect. Dis. **44**:169 (March) 1929.

25. Castellani, A.: Brit. J. Dermat. **42**:365, 1930.

5 *A*). Under ordinary cultural conditions no actively budding stage is observed, and no asci have been found.

Cultural Characteristics.—In culture this fungus may assume a variety of forms depending on the medium, the temperature of incubation, the length of time since its original isolation and the frequency of transfer. The fungus grows well at room or incubator temperature on sugar-containing mediums of a wide range of p_H. It grows feebly on nutrient agar without sugar. It can often be isolated easily from the miliary abscesses at the growing edge of lesions, but may be difficult to recover from older lesions, especially in secondary infections. It usually takes from ten days to two weeks for the organism to appear.

On Sabouraud's maltose agar and similar mediums the fungus slowly forms a downy or fluffy colony with an abundant aerial mycelium, at first white but later often deep cream or tan (fig. 4). In giant colonies the central zone may show radial folds, and concentric rings often occur, giving the colony a resemblance to the trichophytons. There is no formation of gas in sugar mediums. Gelatin and blood serum are liquefied.

Variations in Form.—Henrici [26] referred to three forms of growth: a "mealy" type without aerial mycelium, a prickly type in which the surface is covered with spiny elevations resembling coraemia, and the woolly type just described. The emphasis laid by many authors on the first type is probably responsible for their confusing this fungus with Cryptococcus hominis.

On the glycerin agar medium recommended by Moore [27] the fungus grows rather slowly, forming a heaped-up waxy growth, similar to Henrici's "mealy" type. In these cultures the mycelium increases in diameter, is irregular and tortuous and becomes filled with granules, many of which, when stained with sudan III, are seen to be fat. Thick-walled cells, intercalary, lateral and terminal, are found in great abundance. The characteristic conidia-like bodies may be missed in such cultures. These variations in appearance seem to depend on the conditions of the culture and not on the strain.

Pathogenicity for Animals.—Of the laboratory animals, dogs and monkeys seem to be the most susceptible. Heavy subcutaneous inoculation results in a local suppurating granuloma with metastatic lesions in the lungs and other viscera. Less extensive lesions develop in guinea-pigs.

Other Strains.—Comparative observations have been made on strains 352 and 4738 of the American Type Culture Collection, and also on

26. Henrici, A. T.: Molds, Yeasts and Actinomycetes, New York, John Wiley & Sons, Inc., 1930.

27. Moore, M.: Ann. Missouri Bot. Garden **20**:471, 1933.

the following: (1) a strain isolated by Blankenhorn and Gammel [28] and named by Pollacci and Nannizzi—Glenospora Gammeli; (2), a strain described by Castellani [25] as Blastomycoides tulanensis and later renamed by Agostini—Monosporium tulanense,[29] (3) a strain described by Rewbridge, Dodge and Ayers [30] as Endomyces capsulatus; (4) a strain isolated by MacBryde and Thompson [31] and called by Moore Endomyces capsulatus var. Isabellinus, and (5) another strain described by Moore [32] as Endomyces dermatitidis.

All showed the downy type of colony and the conidia-like bodies described by Gilchrist. In inoculated guinea-pigs all showed the same type of budding cells. In tissue there was some variation in the size of the cells and in culture in the shade of the colonies. Otherwise all these strains appeared identical. No asci could be found either in the cultures of the strains of Endomyces or in the stained sections of E. capsulatus which Moore sent to this laboratory. For the present it seems best to classify them all in the species described by Gilchrist.

The strain named by Castellani Blastomycoides lanuginosus and later renamed Glenospora lanuginosus by Agostini [33] is distinct in its appearance both in culture and in animal tissues.

Terminology.—It seems clear from the quoted description of Gilchrist that the fungi just described are of the species discovered by Gilchrist and that those described by Castellani as Geotrichum (Blastomycoides) dermatitidis [34] and by Ota and Kawatsure as Scopulariopsis Americana [35] belong in other categories.

The relationship of this fungus to other known species is as yet uncertain. The name Blastomyces dermatitidis originally given to the organism by Gilchrist and Stokes has gained such currency that it seems wise to retain it, at least for the present. It would also prevent confusion if the term blastomycosis was reserved for infections with this species and not applied to diseases caused by unrelated fungi.

TYPE III: COCCIDIOIDES IMMITIS (RIXFORD AND GILCHRIST, 1896)

Coccidioidal Granuloma.—The disease coccidioidal granuloma was first reported by Wernicke of Buenos Aires in 1892.[36] A more detailed

28. Blankenhorn, M. A., and Gammel, J. A.: J. Clin. Investigation **4**:471, 1927.
29. Agostini, A.: J. Trop. Med. **35**:266, 1932.
30. Rewbridge, A. G.; Dodge, C. W., and Ayers, T. T.: Am. J. Path. **5**:349, 1929.
31. MacBryde, C. M., and Thompson, E. I.: Arch. Dermat. & Syph. **27**:49, 1933.
32. Moore, M.: Ann. Missouri Bot. Garden **20**:79, 1933.
33. Agostini, A.: J. Trop. Med. **34**:287, 1931.
34. Castellani, A.: Med. Press & Cir. **135**:439 (May 31) 1933.
35. Ota, M., and Kawatsure, S.: Arch. f. Dermat. u. Syph. **169**:149, 1933.
36. Wernicke, R.: Zentralbl. f. Bakt. **12**:859, 1892.

description of the case was given by Posadas [37] in 1900. The condition resembled mycosis fungoides. During the patient's life a large number of parasites believed to be protozoa were found. In 1896 Rixford and Gilchrist [38] studied two cases originating in the San Joaquin Valley in California which they called a protozoan (coccidioidal) infection. In 1900 Ophüls and Moffit [39] assisted by Ash cultivated the parasite, which proved to be a fungus, developing an aerial mycelium.

The character of the lesions and the clinical course of this infection are varied. Ophüls [40] reported that at autopsy a pulmonary focus is nearly always found, and he believed that the majority of cases originate as respiratory infections. The skin and subcutaneous tissues are most frequently involved. The lesions may be firm or soft nodules, ulcers, abscesses or sinuses leading to lesions in the lymph nodes or bones. Involvement of the bones and joints is next in frequency, but the brain, cord, meninges and all the viscera except the gastro-intestinal tract have been known to be involved. The infection may run an acute febrile course with a fatal termination in a few months, but it is usually insidious and of long standing.

The Fungus.—A strain isolated from a typical case of coccidioidal granuloma in Los Angeles was obtained from Dr. John Kessel. A second strain labeled Blastomycoides inmitis was obtained from Sir Aldo Castellani. As seen in the tissues of inoculated animals, these strains correspond well to the original descriptions of Wernicke and Posadas and of Rixford and Gilchrist.

Morphologic Characteristics.—In tissue or pus from inoculated guinea-pigs the parasite appeared as rounded or spherical cells varying in diameter from 5 to 50 microns (figs. 9 and 12). No buds were seen. There was no mycelium. The fungus multiplies by the formation of small bodies within the larger cells which rupture and permit their escape. Two types of the rupturing cells were seen: cells of from 20 to 30 microns filled with innumerable minute particles which are discharged and then develop a visible wall and come to resemble the parent cell, and larger cells from 40 to 50 or more microns in diameter which are frequently covered with numerous radial spines. These contain many sporelike bodies which increase in diameter to 4 or 5 microns and acquire a visible wall while still within the mother cell.

In Culture: The fungus forms a branching coarse mycelium with few septums (fig. 8 *A*). There are no buds or conidia, but the mycelium breaks up into segments of varying lengths. The segments may become

37. Posadas, A.: Rev. de chir., Paris **21**:277, 1900.
38. Rixford, E., and Gilchrist, T. C.: Johns Hopkins Hosp. Rep. **1**:209, 1896.
39. Ophüls, W., and Moffit, H. C.: Philadelphia M. J. **5**:1471, 1900.
40. Ophüls, W.: J. Exper. Med. **6**:443, 1901-1905.

thick-walled and are of the nature of chlamydospores (fig. 8 *B*). A racquet mycelium may be noted (fig. 8 *C*).

Cultural Characteristics.—In culture Coccidioides immitis may resemble the various types of growth observed in Blastomyces dermatitidis, but it usually develops an abundant grayish-white cottony aerial mycelium (fig. 7). The strains studied form a greenish-black pigment on Sabouraud's honey agar and a black pigment on mannitol agar, which Castellani regards as a point differentiating them from Blastomyces. Observers agree as to the rapid liquefaction of gelatin and the absence of gas formation in sugars.

Pathogenicity for Animals.—The fungus is regularly pathogenic for rabbits and guinea-pigs on intraperitoneal or subcutaneous inoculation. After many years on artificial mediums it still reproduces the disease in animals.

The differentiation between Coccidioides immitis and Blastomyces dermatitidis was sharply drawn in the original papers of Rixford and Gilchrist and of Gilchrist and Stokes. The differentiation is made clear by the appearance of these two fungi in the lesions of patients and in those of inoculated animals.

Other Strains.—A culture labeled Blastomycoides dermatitidis and isolated from a cutaneous lesion resembling Gilchrist's disease was received from Castellani with another culture labeled Glenospora meteuropea, also isolated from cutaneous lesions. A third culture, no. 1136, received from Weidman was named Scopulariopsis americana by Ota and Kawatsure. When inoculated subcutaneously into guinea-pigs each of these strains produced spherical cells containing numerous spores of the same type as those produced by the strains of Coccidioides. The appearance and morphologic characters were similar, but in Glenospora meteuropea and Scopulariopsis americana no. 1136 the chlamydospores produced by fragmentation of the mycelium were more uniform in size and shape and Geotrichum (Blastomycoides) dermatitidis failed to produce pigment on mannitol agar. It seems clear that these strains, if not identical with, are at least closely related to, Coccidioides immitis.

Terminology.—Brumpt [41] places Coccidioides immitis among Oomycetes on account of the resemblance of the spore sacs to the sporangia of some members of this order. Many different names have been given to the fungus, but there at present appears to be no valid reason for rejecting that given by Rixford and Gilchrist, Coccidioides immitis.

SUMMARY

Three important types of mycotic infection—cryptococcosis, blastomycosis and coccidioidal granuloma—have been described. Each is a

41. Brumpt, E.: Précis de parasitologie, Paris, Masson & Cie, 1927, p. 1383.

distinct disease etiologically. The infections may be diagnosed by the characteristic picture of the fungus in the lesions, and this diagnosis confirmed by culture. The differential characteristics of the three fungi

TABLE 1.—*Differential Characteristics of Cryptococcus Hominis, Blastomyces Dermatitidis and Coccidioides Immitis*

Fungus	C. hominis (Vuillemin) Cause of cryptococcosis (European blastomycosis, torula infection or torula meningitis)	B. dermatitidis (Gilchrist and Stokes) Cause of American blastomycosis (Gilchrist's disease)	Coccidioides immitis (Rixford and Gilchrist) Cause of Coccidioidal granuloma (California disease)
Morphologic characteristics	In lesion, encapsulated budding, thick-walled cells usually 5 to 8 microns in diameter; occasionally 10 to 15 microns	In lesion, round, budding, thick-walled cells 8 to 20 microns in diameter; no capsule	In lesion, round thick-walled cells, varying sizes 6 to 10 to 50 microns in diameter; no budding; endospore formation; surface of cells often spiny
	In cultures, rounded budding, capsulated cells 4 to 5 microns in diameter; no mycelium; no spores	In cultures, mycelial growth; conidia and chlamydospores; racquet mycelium	In cultures, mycelial growth; no conidia, intercalary chlamydospores; racquet mycelium
Cultural characteristics	At first cream-colored, later yellow to brown, smooth, moist, mucoid colony	At first smooth grayish growth; later aerial mycelium white to tan, downy or fluffy colony; radial folds and concentric rings; sometimes spiny growth	At first smooth grayish growth; later grayish-white fluffy growth; occasionally spiny growth
Identical or closely related species	T. histolytica (Stoddard and Cutler) Saccharomyces tumefaciens (Curtis) Busse Saccharomyces Blanchardi (Blanchard) Guiart Torulopsis hominis var. hondurianus Castellani	Glenospora Gammeli (Blankenhorn and Gammel) Pollacci and Nannizzi Monosporium tulanense (Castellani) Agostini E. capsulatus, Rewbridge, Dodge and Ayers E. capsulatus var. Isabellinus (MacBryde and Thompson) Moore E. dermatitidis (Gilchrist) Moore n. comb.	Geotrichum immitis (Castellani) Agostini Geotrichum dermatitidis (Castellani) Agostini Glenospora meteuropea Castellani Scopulariopsis americana (Ota and Kawatsure)

TABLE 2.—*Diseases in which the Causative Organism Appears in the Lesions as Rounded Cells*

Disease	Described by	Fungus
Histoplasmosis	Darling, 1908	Histoplasma capsulatum
Lymphangitis epizootica	Tokishige, 1896	Cryptococcus farciminosus
Chromoblastomycosis	Lane and Medlar, 1915	Phialophora verrucosa
Chromoblastomycosis	Pedroso, 1911	Hormodendron Pedrosoi
Rhinosporidiosis	Seeber, 1900	Rhinosporidium Seeberi
Sporotrichosis	Schenck, 1898	Sporotrichum Schencki
Systemic moniliasis	Smith and Sano, 1933	Monilia albicans

—Cryptococcus hominis, Blastomyces dermatitidis and Coccidioides immitis—are shown in table 1. For the sake of clearness it should be stated that in addition to these three fungi there are at least seven others which may cause systemic infections with granulomatous lesions and which appear in the infected tissue as rounded cells more or less resembling yeasts; these are listed in table 2.

T. histolytica, Glenospora Gammeli, Monosporium tulanense, E. capsulatus, Geotrichum (Blastomycoides) dermatitidis, Scopulariopsis americana and probably other strains reported under various names seem indistinguishable from one or another of the three types here described. For the recognition and identification of these fungi it is necessary to observe their morphologic characteristics both in the tissue of the host and in culture, their cultural characteristics, and in the case of the first type, their serologic reactions.

CUTANEOUS LEISHMANIASIS

REPORT OF TWO CASES

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NEW HAVEN, CONN.

Cutaneous leishmaniasis, a disease of the orient, is seldom seen in this country, but occasionally cases appear in persons who have recently immigrated from Asia, the countries bordering the Mediterranean, or South America. It is characterized by a lesion of the skin, consisting of a papule or furuncle which later develops into an ulcer, without systemic effect. Many terms have been used for this lesion: oriental boil or sore, Aleppo boil, Delhi boil, endemic boil of the tropics, boil of Biskra, boil of Bagdad and several others. In every case the same pathologic agent has been found, namely, Leishmania tropica. A case recently came under my observation in New Haven, and another case can be found in the records of the New Haven Hospital.

REPORT OF CASES

CASE 1.—During the midsummer of 1921 an Armenian lad, aged 16, who had come to America eight months before reported that three months after his arrival he noticed a small furuncle on the anterior outer aspect of the leg a short distance above the ankle joint. The furuncle was opened by the patient's family physician, and a small amount of purulent material was obtained. The wound failed to heal and ulcerated. The patient was a normal, healthy youth of 16; the lesion on the leg was about the size of a silver half-dollar and had a round, elevated margin and a bright red, granulating bed. There was a moderate amount of seropurulent discharge. Microscopic studies demonstrated the presence of Leishmania tropica. Treatment consisted of roentgen therapy and compresses saturated with surgical solution of chlorinated soda. After some improvement a skin graft was applied to the area, and within from three to four months the lesion healed without complication.

CASE 2.—This case presented a more difficult problem. During the summer of 1930 a girl, aged 10 years, came under my observation complaining of an intractable ulcer on the left shoulder. While living in Palestine she had been bitten on the shoulder by a fly. A few days later a slightly red, indurated area, which was not particularly tender, appeared. It persisted and finally ulcerated. Her family sought the advice of a local physician in Palestine and, failing to find a remedy, came to this country. The patient was healthy and well nourished. The local lesion on the left shoulder had been treated by a number of physicians, almost every conceivable means of cure having been employed. There was a bright, granulating surface from 4 to 5 inches (10 to 12 cm.) in diameter, along one border of which was a ragged, elevated, ulcerating lesion which progressed slowly. A diagnosis of oriental sore was made, Leishmania tropica being found in the microscopic sections.

Fig. 1 (case 1).—Typical cutaneous lesion caused by Leishmania tropica.

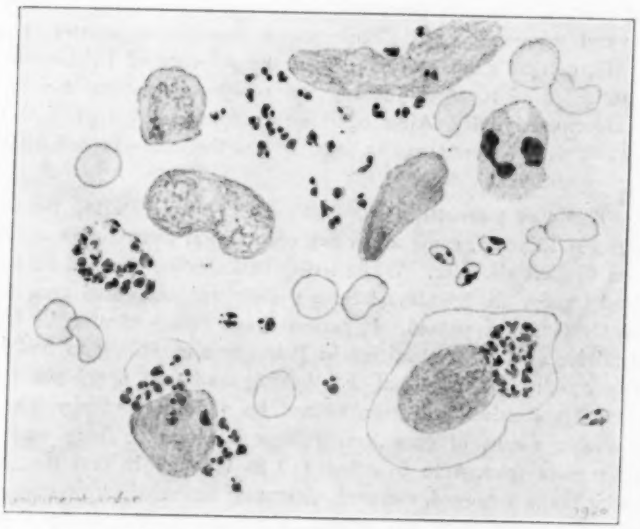

Fig. 2 (case 1).—Leishmania tropica.

Fig. 3 (case 1).—Leishmania tropica, showing the intracellular distribution.

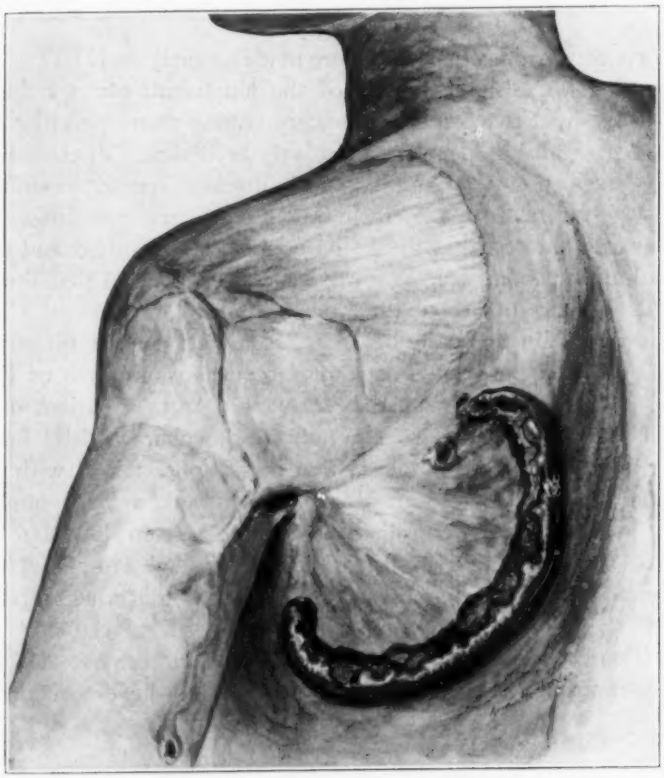

Fig. 4 (case 2).—Lesion showing the atypical formation of the ulceration.

Various types of treatment were employed. Following the advice of many physicians that expectant treatment was best, the wound was left alone and allowed to dry up, but without success. Intravenous injections of emetine hydrochloride had no effect. Compresses of saline solution, surgical solution of chlorinated soda, boric acid, copper sulphate and corrosive mercuric chloride were used without improvement. Silver nitrate, phenol and alcohol were also used. In 1931, an attempt was made to excise the lesion, but it shortly recurred. In retrospect, I believe that the failure at that time was due largely to the small margin which was allowed around the ulcer, which permitted some of the pathologic agents to remain in the connective tissue. As time went on, the lesion progressed with a ragged edge posteriorly over and down the shoulder, leaving in its wake the thick and pink-tinged cicatricial tissue particularly characteristic of this lesion.

In June 1932 the lesion extended from the top of the scapula diagonally to a point directly beneath the left axilla, and excision was again advised, although I realized that the area was the size of a hand. At this time the technic was slightly changed. The ulcer was sealed with collodion and gauze, the skin was thoroughly cleansed and the lesion was excised with an electrocautery, the incision being carried completely around the lesion with a margin of almost 1 inch (2.5 cm.). Dissection was carried through along the fascia, the ulcer being completely excised. The wound was packed, and after a few days, when bright granulations had formed, skin was grafted. Healing progressed without incident, and the patient was discharged. It was interesting to note that in the two years during which the patient was intermittently under my care, she was in excellent general health and developed rapidly.

ETIOLOGY

Reports concerning the lesion were made as early as 1756 (A. Russel and Hasselquist). In the middle of the nineteenth century the lesion was observed by French medical officers among men operating against the tribes of southern Algeria, particularly at Biskra. Their experience is well described by Poggioli. The disease spread rapidly until virtually the entire company, including the officers, was infected. In 1880, Laveran showed that the lesion could be transmitted and that the fly played an important rôle as a carrier. He suggested that the pathologic agent was in all probability a bacterium. The work of Cunningham, a physician in the army of India, seems of some significance. In 1885 he described the results of a microscopic examination of the contents of a "Delhi boil" that had been excised from a patient in Delhi. The boil had not ulcerated. He noticed the characteristic histologic picture of the tissue, and observed that in sections stained with gentian violet and then decolorized in alcohol there were a large number of peculiar bodies varying considerably in size (from 12.8 by 25.6 to 6.4 by 6.4 microns) and in form. He concluded after careful consideration of their various forms and features that they represented different stages of some simple organism of mycetozoic nature. Although objections have been raised as to the correctness of Cunningham's observations, it seems possible that he may have seen the actual pathologic agent.

In May 1903 Leishman first described the protozoon which is the pathologic agent of kala-azar; his report was followed closely by Donovan's independent report in July confirming Leishman's description. This protozoon is now known as Leishmania Donovani. The same month that Donovan described the etiologic agent of kala-azar an Armenian entered the Massachusetts General Hospital in Boston in the service of Dr. Greenough. The lesion which he presented was diagnosed as tropical ulcer by Dr. White; it was excised and curretted, and the tissue was turned over to Dr. Wright, then director of the clinical pathologic laboratory. He made histologic studies and found the typical organism which is now called Leishmania tropica and which is the pathologic agent of oriental sore.

PATHOLOGY

Tropical ulcer usually occurs on the exposed parts of the body, most commonly on the face. The period of incubation is from fifteen days to seven months. The lesion develops in three stages. The first shows a small red, hyperemic area resembling an insect bite. A head develops, which finally discharges a seropurulent fluid. In some instances these cases present a hard tubercle, usually indolent, with little inflammation. The second period is characterized by the formation of ulceration. A typical ulcer has a round, elevated and slightly indurated edge. The bed or crater of the ulcer shows bright red granulation tissue. There is a yellow discharge which, if allowed to dry, forms a thick, hard crust. The edge of the ulcer is often ragged, forming an irregular purple border. There is slight induration, with elevation of the border of the ulcer. The ulcers vary in size and shape. Usually they are oval and from 8 to 10 cm. in diameter. Often under treatment the lesion may spread out and become fan-shaped. Cases have been reported in which the lesion reached the size of one's palm. The third period is the terminal period, during which the ulcer heals and after which cicatricial tissue forms. In the case of large ulcers scar tissue may form in the center first and then around the outer border. The total duration of a lesion is from three months to two years or longer. Many times multiple lesions appear on the face and hands. Although most patients have from 1 to 10 lesions, as many as 174 were reported in 1 instance.

Occasionally complications arise, the most common being a secondary infection with lymphangitis and acute adenitis. Erysipelas is also a common complication. Phlebitis is sometimes seen. Neligun reported a case complicated by tetanus. Scars about the face sometimes cause ectropion or deformities of the nose and mouth, and reconstructive operations are required.

The pathologic agent is Leishmania tropica, a protozoon. It exists in flagellate and nonflagellate forms. When Leishmania tropica is found in the ordinary lesion, the nonflagellate form appears, but under cultural growth flagellate forms are seen. The micro-organisms are round or oval bodies, from about 2 to 4 microns in size, having an eccentric nucleus and another small, rodlike chromatin body. With Wright's stain the protoplasm is colored light blue and the nucleus lilac. Reproduction takes place by cell division. The micro-organisms are often found in great numbers in the large mononuclear cells—up to 100 in a cell. Morphologically, the organisms on smears are indistinguishable from two other protozoa, Leishmania Donovani and Leishmania americana, except that Leishmania tropica has more of a tendency to flagellate formation in culture than has Leishmania Donovani. Fox pointed out that the American leishmania differs in the gross appearance of the cultures on solid mediums. Noguchi showed by agglutination tests that there is a definite immunologic difference.

These protozoa, however, are clearly distinguished clinically by the characteristic disease entities which they produce. Leishmania Donovani causes kala-azar; Leishmania tropica, oriental sore; Leishmania americana or braziliensis, American leishmaniasis.

Kala-azar, or tropical sphenomegaly, is a chronic febrile disease. It occurs in epidemics characterized by chronicity, irregular fever, pigmentation of the skin and enlargement of the liver and spleen. A high mortality exists. Clinically, the disease is ushered in with rigor and irregular fever. A lower fever follows and gradually declines. The skin takes on an earthy color. The spleen is firm and greatly enlarged. Hemorrhages in any tissue are to be expected. The blood shows a secondary anemia and leukopenia, with a relative predominance of mononuclear cells and lymphocytes. Cachexia and wasting become increasingly marked. After many months death results from asthenia or intercurrent disease.

Leishmania tropica and Leishmania americana are more difficult to distinguish but have been differentiated by the anatomic area in which they occur and by clinical and immunologic features. Leishmania americana causes a lesion found frequently on the mucous membranes of the nose, pharynx and mouth. Leishmania tropica is found on the exposed surfaces, such as the skin of the face, the anus, the hands and the feet. American leishmaniasis has a varied and much longer course than oriental sore. One lesion of oriental sore will produce immunity, while in American leishmaniasis no immunity is produced. American leishmaniasis also has a greater resistance to treatment and occasionally causes cachexia and death. Oriental sore is milder and invariably causes immunity but never death.

The lesion may occur at any season of the year, but is most frequently seen during the autumn. The history of most patients shows

that the initial lesion was caused by the bite of a fly. The mode of transmission consists in the fly's sucking the blood and then excreting intestinal contents on the skin, thus causing inoculation. If the lesions are exposed to the fly, transmission can take place readily, and the infection will spread rapidly. The geographic distribution is interesting. The lesion occurs usually in tropical countries, being found principally in southern and western Asia and in the countries bordering the Mediterranean. Strangely, in India one finds Leishmania tropica in the western part and kala-azar in the eastern section. Cases have been reported in China. Leishmania americana is found in South America on the eastern slopes of the Andes and in New Mexico, Yucatan and the West Indies. Occasional cases are seen elsewhere, but usually in people who have come from the districts in which the lesion is most commonly found.

The diagnosis is made from the characteristic history and appearance of the lesion and by the finding of protozoa in microscopic examination. The organisms are best obtained by aspirating a nonulcerating, early lesion. In the later stages the organisms can be found best in scrapings from along the margin of the ulcer or in the microscopic examination of excised tissue. The observation of these bodies makes the diagnosis certain.

PROGNOSIS AND TREATMENT

The lesion usually heals in from three months to two or three years. It is seldom serious because of its local involvement and, unless complications set in, is seldom fatal.

Although many forms of treatment have been used, most authors consider expectant treatment the best. The ulcers in most cases have been found to heal spontaneously in from three months to two or three years. The Arabs apparently for years have recognized the value of treating the lesion in this way, because one finds that they assist the drying with the use of a dusting powder, which forms a scab. They protect the lesion from trauma and find after a time that the tropical cicatrix, which is so striking in this disease, has formed beneath the scab.

Many types of medication have been used, but most of them unsuccessfully. Mitchell reports that he treated 300 patients with phenol and alcohol, with some favorable results. Silver nitrate has been reported as being of value. Potassium permanganate has been used with satisfactory results. Nicol gave arsphenamine intramuscularly, and reported good results in 2 cases. The use of surgical solution of chlorinated soda has met with slight success. Antimony and potassium tartrate has been employed with considerable success.

Cauterization with the actual cautery has been found to produce considerable pain and seems to aggravate rather than help the condition.

Roentgen therapy has been reported to have a favorable action on the lesion, and in case 1 apparently had a valuable therapeutic effect.

Excision of the lesion, particularly when the position of the ulcer is favorable, has been performed successfully. Bussière and Nattan-Larrier stated that it is the treatment of choice and laid emphasis on the fact that in excising the ulcer a margin of at least 20 mm. around the ulcer must be left because of the presence of Leishmania in the subcutaneous tissue. This treatment was used successfully in case 2, and I believe that in cases in which excision with the electrocautery is possible it is of definite value.

The drawings for case 1 were loaned to me by Dr. Raymond Hussey, of the Department of Pathology, Yale University School of Medicine.

BIBLIOGRAPHY

Andrews, J. M.: Report of a Case of Oriental Sore in United States, Am. J. Trop. Med. **7**:221 (July) 1927.

Cope, Zachary: Clinical Types of Bagdad Boil, Brit. J. Surg. **8**:259 (Jan.) 1921.

Craig, C. F.: Parasitic Protozoa of Man, Philadelphia, J. B. Lippincott Company, 1926, p. 340.

Escomel, E.: La leishmaniose americaine et les leishmanioses en Amerique, Bull. Soc. path. exot. **22**:35, 1929.

Faber, H. K., and Schussler, H. Jr.: Leishmaniasis in the United States, J. A. M. A. **80**:93 (Jan. 13) 1922.

Fox, H.: Two Cases of Oriental Sore, New York M. J. **116**:57 (Oct. 4) 1922.

Hasselquist, F.: Medical, Chirurgical and Anatomical Cases, London, 1758, p. 189.

Hegner, R. W., and Taliaferro, W. H.: Human Protozoology, New York, The Macmillan Company, 1924.

Heydenreich, L.: Le clou de Pendeh; analyse du travail par Duclaux, Ann. Inst. Pasteur **3**:455, 1889. Le clou de Pendeh, St. Petersburg, I. Treĭ, 1888, vol. 1, with atlas.

Klotz, O., and Lindenberg, H.: The Pathology of Leishmaniasis of the Nose, Am. J. Trop. Med. **3**:117 (March) 1923.

Laveran, A.: Leishmanioses, Paris, Masson & Cie, 1917.

Leishman, W. B.: Quart. J. Med. **5**:109 (Oct.) 1911.

McEwen, E. L.: Oriental Sore in the Americas, J. Cutan. Dis. **32**:275 (April) 1914.

Mayer, M., and Ray, J. C.: Zuchtung und Differentialdiagnose verschiedener Leishmanien (Kala-azar, orientbeule und brasilianische Leishmaniose) auf festen Nährböen, Arch. f. Schiffs- u. Tropen-Hyg. **32**:277 (June) 1928.

Nattan-Larrier, L., and Bussière, A.: Bull. Soc. path. exot. **2**:26 (Jan.) 1909.

Noguchi, H.: Action of Certain Biological, Chemical and Physical Agents upon Cultures of Leishmania; Some Observations on Plant and Insect Herpetomonads, Internat. Confer. Health Prob. in Trop. America, Boston, United Fruit Company, 1924.

——and Lindenberg, A.: The Isolation and Maintenance of Leishmania on the Medium Employed for the Cultivation of Organisms of the Leptospira Group of Spirochetes, Am. J. Trop. Med. **5**:63 (Jan.) 1925.

Poggioli, P. J.: Thèse inaugurale, Paris, 1847.

Smith, D. K.: Oriental Sore, Arch. Dermat. & Syph. **5**:69 (Jan.) 1922.

Wright, J. H.: Protozoa in a Case of Tropical Ulcer ("Delhi Sore"), J. M. Research **5**:472, 1903-1904.

GLOSSITIS RHOMBICA MEDIANA

REPORT OF A CASE WITH RESULTS OF TREATMENT

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The lesion of the tongue known as glossitis rhombica mediana was first described in 1914 by Brocq and Pautrier[1] under the name of "glossite losangique médiane de la face dorsale de la langue." Since their description was published, relatively few articles on the condition have appeared in the literature. It therefore seems appropriate to report a case that has recently come under my observation. This case is of interest as a reminder of the clinical picture and of the fact, as pointed out by Dubreuil,[2] that the lesion may be mistaken for a manifestation of syphilis. The comprehensive appellation glossitis rhombica mediana was given to the lesion by Lane[3] in 1924. A review of the existent literature was included in his article.

Clinically, the picture is that of a roughly rhomboid or oval, smooth or lobulated patch situated on the dorsum of the tongue just anterior to the V formed by the circumvallate papillae. The long axis lies in the median raphe. The typical lesions are lozenge-shaped, but there are other types. The papillae are absent in the area, the surface being either smooth or covered with nodular elevations separated at times by apparently deep fissures. Nodules, when present, are yellowish and scattered or grouped at the center of the lesion. The borders of the lesion may be distinct or blend with the surrounding normal tissue. Infiltration in the subjacent tissue is evidenced by slight induration. Subjective symptoms are absent except for occasional burning or tingling. The patient is usually made aware of the condition by accident or through examination by his physician.

REPORT OF A CASE

History.—M. H., a man, aged 55, presented himself at the clinic complaining of a growth on his tongue. He had experienced no discomfort from the lesion; in fact, his attention was called to it by a dentist. Slight apprehension regarding its nature had prompted him to visit the clinic. The patient had always enjoyed

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From the service of Dr. Herman Goodman, the Stuyvesant Square Hospital, formerly the New York Skin and Cancer Hospital.

1. Brocq, L., and Pautrier, L. M.: Glossite losangique médiane de la face dorsale de la langue, Ann. de dermat. et syph. **5**:1, 1914.

2. Dubreuil, W.: Glossite médiane de la face dorsale de la langue, Ann. de dermat. et syph. **5**:615, 1914-1915.

3. Lane, J. E.: Glossitis Rhombica Mediana, Arch. Dermat. & Syph. **9**:547 (May) 1924.

good health. There was no history of venereal infection. The Wassermann test was negative.

Clinical Examination.—On the dorsum of the tongue there was a roughly diamond-shaped, slightly elevated lesion measuring 1.5 by 2 cm. (fig. 1). The

Fig. 1.—Diamond-shaped lesion on the tongue, showing slight mamillation and reddening.

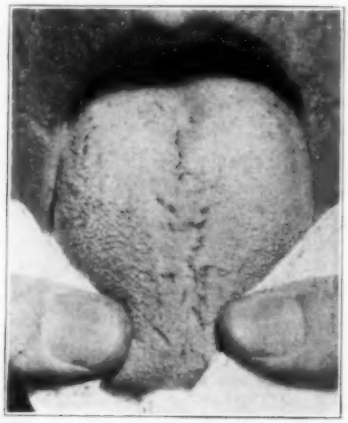

Fig. 2.—Condition of the tongue seven months after treatment.

surface of the lesion was slightly mamillated and reddened. The border was fairly distinct. There was slight induration, and sensation in the area was normal. The remainder of the dorsal surface of the tongue was somewhat coated.

Pathologic Changes.—Microscopic examination showed an irregular acanthosis. The stratum corneum was absent over most of the area, the portion present showing parakeratosis. The stratum granulosum was absent. An infiltration of small

lymphocytes and new connective tissue cells was noted in the corium about the blood vessels as well as in nodular masses. The connective tissue in the mid-corium presented broad, homogeneous staining bands with few nuclei, which is evidence of the sclerosis one finds in this condition.

Treatment.—The tongue was anesthetized with procaine hydrochloride and the lesion desiccated with the fulgurating current, the dry tissue being removed with a curet. No recurrence was noted after seven months (fig. 2).

SUMMARY

1. A typical case of glossitis rhombica mediana with the characteristic microscopic changes is reported.

2. Superficial desiccation and curettage afford a reliable method of treating these lesions.

Second Avenue and Nineteenth Street.

DARIER'S DISEASE WITH FATAL RADIUM DERMATITIS

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REPORT OF A CASE

R. R., an unmarried woman, aged 73, from the Calle farm at Penjamo, State of Guanajuato, had no hereditary taint. Her grandparents had lived to old age. Her father died of pneumonia and her mother of acute enteritis. She had two brothers and four sisters, one of the brothers dying at birth, which occurred while the mother was suffering from exanthematic typhus. The other brother died in old age of arteriosclerosis. Two of the sisters died insane. The third sister succumbed to malarial cachexia and the fourth died of generalized adenosarcomatosis. None of her relatives had suffered from Darier's disease.

The patient had previously suffered from measles, tertian malaria, repeated attacks of amebic dysentery during many years, repeated attacks of erysipelas on various parts of the body including the face, fracture of the fibula which healed normally and, in 1920, severe atypical ambulatory typhoid fever. Aside from this the patient was entirely normal, of forceful character, well balanced, rational and capable in all that she undertook. She presented no stigmas of degeneration. The menses and menopause had been normal.

The follicular dyskeratosis began in adolescence following measles. The patient presented a typical appearance, with dark, greasy skin, lesions that were crusted, follicular, brown, umbilicated and horny, and plugs at the mouth of the follicles in the form of soft, yellowish masses with a characteristic bad odor. The sites occupied by the lesions were classic: the temples, ears, submammary, axillary and inguinal folds and anterior and posterior mediothoracic regions, in which the hyperkeratotic cones were large, abundant and almost confluent.

On the backs of the hands were papules with the appearance of flat warts, a characteristic of the disease. On the external and dorsal aspect of the feet and in the right inner malleolar region there were brownish-red, cauliflower-like vegetations with a fetid odor which were rebellious to all treatment. As is the rule, the scalp showed large, hyperkeratotic, whitish crusts without a fall of hair.

The most interesting point in the history of this case was the plantar keratosis which appeared early and which gradually progressed until it caused an inflexible, hard sole, which made walking difficult and painful. In 1926 a fissure appeared on the plantar surface and gradually increased in size and depth, causing excessive pain which made walking almost impossible. A second fissure with the same characteristics formed rapidly in the neighborhood of the first. In both, the characteristic bad odor of the dermatosis was pronounced. None of the treatments usually employed for fissures gave satisfactory results. Healing was not possible, as the lesions were situated in the depth of a horny layer about 2 cm. thick. Dr. Rosendo Amor E., a distinguished surgeon, even suggested amputation of the foot.

Translated by Howard Fox, M.D.

In this desperate situation it was thought that an application of radium might cure the keratosis and the fissures at the same time. A gynecologist who used radium was consulted. He thought that the plantar keratosis and the other lesions of the foot would disappear with radium therapy. Accordingly, on Sept. 3, 1927, he applied two tubes of radium to the plantar fissures, a third to the vegetating lesions on the dorsum of the foot and a fourth to similar lesions on the malleolus. All together four tubes, the strength of which was unknown, were applied without filtration in a single seance of about six or seven hours. At the end of forty-eight hours radium dermatitis appeared, which was almost phlegmonous and included the entire irradiated extremity. It caused the formation of an abscess on the great toe and three extremely painful round ulcers 2 inches (5.08 cm.) in diameter which involved the entire thickness of the skin of the internal malleolus, a situation in which the skin lies directly on the bone and is radiosensitive. The radium dermatitis healed within two months after having caused much pain. The entire hyperkeratotic plantar layer came off like a sandal leaving the skin smooth and soft with cicatrization of the fissures. All seemed to have ended favorably, as the foot appeared normal and caused no discomfort.

Four years later, following a prolonged bath, an ulcer reappeared on the malleolus in the scar of one of the former ulcers, having the same form and extent. This area of radium dermatitis had no tendency to heal, was refractive to all treatment and was painful to the point that the patient could not stand contact with cotton and required local anesthesia of a 2 per cent solution of benzoyl-dimethyl-amino-ethyl propanol hydrochloride when the dressings were changed. The patient, who had stoically borne the greatest pain, burst into tears and nearly fainted when this neuritic ulcer was dressed.

Six months later a similar ulcer occurred in one of the cicatrices. The first ulcer healed for a while, but the other did not. The result of the presence of the two ulcers was a gradual weakness of the entire lower extremity with progressive difficulty in walking and invalidism during the last two years of life.

About four months prior to death edema of the lower extremities appeared, with gradual upward progression. The urine was normal, and the blood showed normal quantities of chlorides and urea. Coincident with the increase of the edema, the urine continued to be concentrated and highly colored. Toward the end of the illness there were unusual disturbances in the digestive tract. Three hours after the principal meal each day false tenesmus occurred, causing at first the passage of a normal stool followed at short intervals by two or three passages of frothy and odorless mucus.

On Jan. 12, 1933, there was pseudoparalysis of the affected leg, at the extremity of which erysipelas made its appearance accompanied by severe chills and fever. The erysipelas became bullous and with the ulcerating radium dermatitis caused such an abundant discharge of serum that it was necessary to change the dressings constantly, which added to the patient's suffering.

The destruction of tissue was so great that the superimposed erysipelas was able in three or four days to cause pseudo-ankylosis in semiflexion of the limb. Eight days before death the erysipelas recurred, this time generalized, with large and painful erythematous patches on the back, making the dorsal position, the only one possible, extremely painful. On March 5 the patient died. Her mind remained clear to the last moment.

The diagnosis was first made in 1902 by Dr. Angel J. Rodriguez, professor of dermatology in the University of Mexico, and was later confirmed by his

successor, Dr. Ricardo E. Cicero. In December 1931, Dr. Joseph J. Eller, an American dermatologist, saw the patient. He recommended excision of the first ulcer, which was completely formed, followed if necessary by skin grafting and electrodesiccation for the second ulcer, which had barely begun. The patient was unwilling to undergo this treatment and I doubted the utility of the destruction of the ulcers, as the entire skin was affected by the radium dermatitis. The skin at the border of the ulcer was, like the rest of the irradiated area, smooth, atrophic, pigmented, telangiectatic and wrinkled, in places resembling the peel of an onion. It would have been impossible to heal ulcers on such a surface.

SUMMARY AND CONCLUSIONS

1. This case of Darier's disease was neither hereditary nor familial.
2. It appeared after an attack of measles.
3. Two sisters of the patient were mental degenerates.
4. The patient's mentality was entirely normal.
5. The disease preserved its benign character except for the severe plantar keratosis and fissures.
6. It presented exacerbations in the spring and became notably better in the winter.

As for the radium dermatitis: (*a*) The immediate phlegmonous and ulcerating stage was serious.

(*b*) The late stage, four years after the application of the radium, was more serious since it produced progressive functional disability of the lower extremity, with two years of invalidism and intense suffering.

(*c*) The final picture of cachexia, independent of the age of the lesion, can be attributed to radium, all the deadly effects of which one does not yet know.

(*d*) Disregarding the radium dermatitis, the action of the radium on the plantar keratosis and fissures was remarkable.

(*e*) My earnest desire is that the publication of this article will prevent similar tragic occurrences.

ARSPHENAMINE DERMATITIS RESEMBLING PITYRIASIS ROSEA

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The cutaneous reactions caused by arsphenamine may, for the sake of convenience, be divided into two groups. To the first group belong all eruptions which are not characterized by scaling, namely, all exanthematous, urticarial and fixed eruptions. The reaction is due to a sensitization of the skin to arsphenamine or its derivatives, and possibly also to the products of metabolism of these drugs. It may be enhanced by a state of general allergy or instability of the patient and is influenced in the same manner as is allergy for other drugs and chemicals by heredity, age, disturbances in metabolism, dysfunction of the endocrine system and disturbances in the autonomic nervous system. A reaction due to allergy does not depend on the arsenic content of the preparation or on the quantity of the drug injected. The same eruption will occur after each injection, no matter how small the dose. Nor is it influenced by the length of the interval between injections. In one patient,[1] a dermatitis occurred after an intradermal injection of 0.3 mg. of neoarsphenamine for test purposes. According to Moore and Keidel,[2] the allergy may, in a certain number of instances, be specific for the preparation employed. For example, neoarsphenamine may be given to a patient who is sensitive to silver arsphenamine. An allergic reaction of the skin never occurs after the first injection; it usually follows a second or third injection, although some patients may tolerate many injections before they become sensitized. The injection which precedes the one causing the eruption acts as the sensitizing agent. The intolerance for the drug may be manifested in a group of symptoms not unlike that of a serum reaction, namely, an attack of urticaria, erythema, angioneurotic edema and vomiting, coming on immediately after the injection, or the reaction may be identical with that which occurs in

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From the Department of Dermatology, Morrisania City Hospital.

1. Moore, J. E.; Woo, S. T.; Robinson, H. M., and Gay, L. N.: Reactions of the Skin Following the Intradermal Injection of Arsphenamine: Postarsphenamine Dermatitis, Arch. Dermat. & Syph. **23**:74 (Jan.) 1931.

2. Moore, J. E., and Keidel, A.: Dermatitis and Allied Reactions Following the Arsenical Treatment of Syphilis, Arch. Int. Med. **27**:716 (June) 1924.

patients who are allergic to the various drugs and chemicals. The eruption may resemble the exanthemas, such as scarlet fever or measles, or it may be of the type which is called a fixed eruption and is identical with that caused by phenolphthalein and antipyrine. In this type of eruption, the lesions recur in exactly the same area or areas after each injection, new lesions being constantly added.

The second group of eruptions due to arsphenamine consists of the scaling dermatoses. Some of these reactions are accompanied by severe disturbances in the blood, liver and kidneys and not infrequently have a fatal termination. They differ in no way from the symptoms caused by arsenic poisoning. In this type of eruption, the attack usually follows a great many injections of arsphenamine, except in the cases in which the preparation is unusually toxic or is decomposed in the ampule. Idiosyncrasy, which, according to Bloch,[3] differs from allergy quantitatively rather than qualitatively (in other words, there is an increased or diminished susceptibility to the normal physiologic action of the drug), may play a part in causing the reaction. As these reactions are accompanied by dysfunction of the liver, one is safe in assuming that retention of arensic in the system contributes to the causation of a reaction in at least some of the cases. Some would have it that even these cases are always due to allergy, arguing that if they were due to toxemia they would be of a more common occurrence. Our view coincides with that of Moore and his co-workers,[1] who believed that both allergy and toxemia participate in the causation of the reaction.

A reaction to arsphenamine may simulate any of the commonly known dermatoses. Lichen planus, psoriasis, herpes and measles have been so cleverly and artistically imitated by reactions to arsphenamine that in many instances it has been difficult to determine whether we were dealing with the real disease or with an imitation. On the other hand, irritants of a diverse nature are capable of producing the identical reaction; for example, syphilis and arsenic are capable of producing keratosis, while syphilis, arsenic and sunburn have been known to produce lichen planus-like eruptions.[4]

The ability of an agent to cause persons to react with a variety of eruptions does not reside in the drug or the physical agent, but is inherent in the person himself. This tendency or diathesis of the patient and the variation in the structure and the constitution of the skin are responsible for the kind of eruption one may react with to

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3. Bloch, B.: The Rôle of Idiosyncrasy and Allergy in Dermatology, Arch. Dermat. & Syph. **19**:175 (Feb.) 1929.

4. About two years ago, one of us (S. F.) observed a patient in whom a lichen planus-like eruption developed after a severe sunburn of the face, neck and extremities. The eruption remained strictly localized within the area not covered by the bathing suit. It became generalized one month later.

irritation. A patient with seborrhea may react differently from one with psoriasis, who reacts to injuries with a new outcrop of psoriasis. Following the use of arsenic, eczema or dermatitis exfoliativa may develop in patients with a tendency to dermatitis, and keratosis follicularis or keratosis palmaris et plantaris may develop in those with a keratoid tendency. Epidermolysis may develop following injury in persons with a tendency to bullous formation, while pigmentation or keloids have a tendency to develop in others. These various reactions are caused by the action of the drug or chemical on the vegetative nervous system. This may be borne out by the fact that an eruption due to arsphenamine occasionally occurs long after treatment with the drug has been discontinued. Harry [5] reported a case in which an eruption appeared during the third course of arsphenamine; it cleared up in ten weeks, remained absent for three weeks and reappeared in spite of the fact that no further treatment had been given. That the structure and the condition of the skin are factors in the production of a drug eruption and in determining its localization may be seen from the following cases. Schneerman [6] reported a case of arsphenamine dermatitis which occurred on the site of a previous sunburn. Galewsky [7] reported a case of circumscribed dermatitis, somewhat scaly, which occurred on the chest of a patient who was treated with silver arsphenamine, but who had previously been exposed to the roentgen rays. The area involved was rectangular, corresponding exactly to the area of exposure. The eruption in the restricted area appeared three weeks after the exposure, but it became generalized a week later. This case vividly illustrates the fact that there are differences in cutaneous susceptibility, that hypersensitiveness may be greater in one region of the body than in another or it may be strictly localized, and also that hypersensitivity may be artificially produced by applying a local irritant to the skin. Jadassohn [8] reported a case in which an irritation of the skin by benzene had caused the first localization of a serious arsphenamine dermatitis.

Concerning the eruptions due to arsphenamine other than the scaling dermatoses, the group of eruptions to which our case belongs, there has been a controversy as to the identity of the eruption due to arsphenamine with those due to other causes. This controversy is particularly active in the case of lichen planus. Buschke and Freymann [9] reported a number

5. Harry, F.: Spontaneously Recurrent Exanthem After Arsphenamine, Dermat. Ztschr. **37**:305, 1923.

6. Schneerman: Arsphenamin Dermatitis Especially Localized on the Site of a Previous Erythema Solare, Arch. Dermat. & Syph. **8**:740 (Nov.) 1923.

7. Galewsky, E.: Roentgen-Ray and Arsphenamine Dermatitis, Dermat. Wchnschr. **73**:817, 1921.

8. Jadassohn, in discussion on Schneerman.[6]

9. Buschke, A., and Freymann, W.: Arsphenamine Eruptions, Med. Klin. **7**:899 (July 24) 1921.

of cases of eruptions following the use of arsphenamine which resembled lichen planus. In some of these cases, the histologic changes were typical of lichen planus. Wirtz [10] reported two cases of lichenoid eruptions following the use of arsphenamine, and stated that the points of similarity between these eruptions and real lichen planus were too few to regard lichen planus as arising from the same cause as the post-arsphenamine eruptions, namely, an attack on the vegetative nervous system. He believed that real lichen planus occurs only as a coincidence. Frei and Taschau [11] did not agree with Wirtz. They reported three cases of lichenoid arsphenamine dermatitis which were indistinguishable from lichen planus. They were unable to regard these frank cases of lichen planus as a mere coincidence. Jadassohn [12] stated that cutaneous reactions to various agents may closely resemble one another, and that lichen planus may be indistinguishable from a lichenoid eruption due to arsphenamine, as true zoster may be identical with the zosteroid eruption caused by arsphenamine.

That arsphenamine is capable of producing zoster-like lesions has never been proved, and, for that reason, the opinion on this subject is not unanimous. In our case of pityriasis rosea following the use of arsphenamine, this proof is actually furnished by the occurrence of the identical eruption after each injection of arsphenamine.

There is no such controversy regarding the cases of psoriasis which were reported as following injections of arsphenamine. These were evidently cases of real psoriasis which were brought on by that drug in patients who had a tendency to psoriasis or in those who had previously suffered from attacks of that disease.

As already stated, arsphenamine eruptions may resemble any of the known dermatoses and be indistinguishable from them. Postarsphenamine exanthems resembling urticaria,[13] angioneurotic edema,[14] generalized erythema,[15] erythema multiforme,[16] measles [17] and purpura haemor-

10. Wirtz, F.: A Contribution to Our Knowledge of the Lichenoid Arsphenamine Eruptions, Dermat. Wchnschr. **75**:1213 (Dec. 13) 1922.

11. Frei and Taschau: Lichen Ruber-Like Arsphenamine Eruptions, Arch. f. Dermat. u. Syph. **141**:152, 1922.

12. Jadassohn, J.: Remarks Concerning Paper by Frei and Taschau, Dermat. Wchnschr. **76**:261 (March 24) 1923.

13. Rosen: Arsphenamin Dermatitis, Arch. Dermat. & Syph. **6**:98 (July) 1922. Lacapore and Lepiney: Localized Eruptions Following Arsphenamine, Bull. Soc. franç. de dermat. et syph. **30**:149, 1923.

14. Guttman, C.: So-Called Fixed and Ordinary Urticarial Recurrent Exanthems, Dermat. Ztschr. **35**:135, 1921. Poland, N.: ibid. **36**:49, 1922.

15. Criado, in discussion on Casal: Arsphenamin Erythroderma, Arch. Dermat. & Syph. **5**:524 (April) 1922.

16. Fox, H.: Palmar Eruption of Erythema Multiforme Type Following Arsphenamin Treatment, Arch. Dermat. & Syph. **8**:439 (Sept.) 1923.

17. Ingram, T. T.: Brit. J. Dermat. **39**:406 (Oct.) 1927.

rhagica [18] have been reported by a number of observers. Hemorrhagic purpura usually occurs as an arsenical toxemia and is accompanied by severe constitutional symptoms and changes in the blood. However, it may also occur as an allergic manifestation, disappearing and reappearing after each injection. Cezare and Duruy [19] reported a case of nitritoid crisis with hemorrhagic purpura which had occurred after several injections of arsphenamine. The treatment was discontinued for eight months and, when it was resumed, there was another nitritoid crisis followed by hemorrhagic purpura four hours later. The fixed arsphenamine eruptions may be indistinguishable from those produced by arsphenamine and antipyrine,[20] or they may be pigmentary in nature.[21] Pemphigus foliaceus following the use of arsphenamine has been reported by Massia.[22]

Pityriasis rosea following the use of arsphenamine has been reported by a number of observers.[23] It is not because of the rarity of this form of eruption or the uniqueness of its appearance that the following case is reported, but because the clinical history of the patient and certain occurrences during the course and the treatment of the disease were so extremely instructive.

REPORT OF A CASE

E. W., a Russian Jewish housewife, aged 45, was transferred from the ophthalmic clinic at Morrisania City Hospital for antisyphilitic treatment on Jan. 18, 1933. She had no children but had had one miscarriage. At the time of her admission, she was past the menopause. She stated that she had been suffering from headaches and pain in the temporal region.

There was periostitis in the region of the lacrimal groove, as evidenced by a swelling near the inner canthus of the right eye. A coloboma of the choroid was present in the right eye. In the left, there were areas of choroiditis and haziness of the vitreous humor, which was filled with floating opacities. The Wassermann reaction was 4 plus; the blood count and differential count were normal, and the hemoglobin was 70 per cent. The patient presented no other evidence of syphilis.

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18. Chatelier, L.: Purpura Haemorrhagica with Fatal Oral Hemorrhage After Arsphenamine, Bull. Soc. franç. de dermat. et syph. **30**:50, 1923.

19. Cesare and Duruy: Postarsphenamine Nitritoid Crisis and Purpura, Bull. Soc. franç. de dermat. et syph. **40**:131 (Jan.) 1933.

20. Levine: Fixed Eruptions with Pigmentation from Arsphenamin, Arch. Dermat. & Syph. **8**:109 (July) 1923. Chargin: Dermatitis Medicamentosa—Phenolphthalein, ibid. **4**:270 (Aug.) 1921.

21. Wise, F.: Fixed Arsphenamin Pigmentation, Arch. Dermat. & Syph. **9**:645 (May) 1924.

22. Massia, G.: A Contribution to the Study of the Arsphenamines, Ann. de dermat. et syph. **4**:145, 1921.

23. Schoenhof: Arsphenamin Dermatitis, Arch. Dermat. & Syph. **9**:277 (Feb.) 1924. Oppenheim: Salvarsen Dermatitis von Pityriasis Roseaähnlichen Character, Dermat. Wchnschr. **82**:651, 1926. Bruhns, quoted by Kerl, W.: Schädigungen durch Salvarsan, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 19, p. 622.

A course of treatment with bismuth and arsphenamine was instituted and, between January 25 and May 15, nine injections of neoarsphenamine were given, each consisting of 0.45 Gm.

After a period of rest of one month, the patient returned for treatment. Her Wassermann reaction was negative. A new course of treatment was started, and on July 19, when the second injection was given, there was a slight infiltration of the perivenous tissue. The assistant in charge of the syphilitic clinic stated that swelling, itching and burning occurred after the accident. The symptoms rapidly subsided after the application of a wet dressing.

On July 26, the patient received an intravenous injection of 0.45 Gm. of neoarsphenamine. On the following day, an eruption appeared on the patient's abdomen and on both arms. The lesions consisted of oblong or rounded patches, ranging in size from that of a lentil to that of a bean or larger. They were pale red with a lighter center and a scaly margin. In some patches, the scale was centrally located, and it was detached at the periphery. The eruption was accompanied by severe itching. In spite of the fact that several of the lesions resembled urticaria and that there was no evidence of a "herald spot," the picture was so strikingly like pityriasis rosea that we were unable to determine whether we were dealing with that disease or whether the eruption was due to arsphenamine. We decided, however, to discontinue the treatment, and the lesions cleared up within four weeks.

On August 23, treatment was resumed, and the patient received 0.2 Gm. of neoarsphenamine, whereupon the eruption promptly reappeared. This time, the individual lesions were somewhat larger and the eruption occupied a larger area, involving the abdomen, thighs and axillae as well as the arms. It presented the same characteristics as the original eruption, but was of shorter duration, having completely disappeared within a week. On November 4, the administration of 0.2 Gm. of neoarsphenamine was again followed by a pityriasis rosea-like eruption, and at this point the question arose as to whether it was safe to continue the administration of arsphenamine. In spite of the fact that pityriasis rosea-like post-arsphenamine eruptions have been reported [23] in which the exanthem had become eczematized, we decided to proceed with caution and to continue the treatment. In order to diminish the chances for a toxic reaction, the dose administered consisted of only 0.15 Gm. of neoarsphenamine. The result, however, was the same, as was also the outcome of an injection of 0.1 Gm. the following week.

On October 4, a patch test was made with a 1:100 solution of the drug which was taken from the same stock as was used in the treatment of the patient. The result was entirely negative. An intradermal injection of 0.2 cc. of a 1:100 solution of neoarsphenamine was given on October 9, and the result was as follows: Within ten minutes after the injection, a marked erythema developed in an area about 2 inches (5 cm.) in diameter immediately surrounding the point of injection, and all pityriasis rosea-like lesions which were present at that time flared up and became acute. The itching sensation, which had completely subsided by that time, recurred, and it was as severe as it was in the early stages of the eruption. New lesions also appeared.

On October 26, a few hours prior to the presentation of the patient at a meeting of the Bronx Dermatological Society, in order to reproduce the eruption for the purpose of demonstration, the patient again received a small dose of neoarsphenamine (0.05 Gm.). At the time of presentation, the eruption had recurred, and the lesions were so numerous that they literally covered the entire body.

In order to ascertain whether the patient's sensitivity was specific for neoarsphenamine, we decided to change the preparation of arsphenamine and injected 0.05 Gm. of silver arsphenamine on December 27. About three hours after the

injection, there was a severe itching followed by an eruption. In appearance, the lesions were identical with those which occurred after the use of neoarsphenamine, but the eruption was even more extensive than it was on the previous occasions. At this point, all arsphenamine medication was ordered discontinued permanently, in the fear that we had reached the threshold of safety.

If the patient was to receive any arsenical medication, some quinquivalent arsenic preparation had to be decided on. Tryparsamide was chosen because it was at hand. An examination of the eyegrounds was made. The optic disks were found to be normal, and areas of healed choroiditis were seen instead of the previously existing active lesions.

On Jan. 17, 1934, the patient received 1 Gm. of tryparsamide without the occurrence of any reaction. This treatment was repeated several times without any mishaps. The patient was finally given acetarsone by mouth. This drug has likewise been well tolerated.

COMMENT

It is of interest that the patient received a whole course of arsphenamine without the occurrence of any reaction. The first eruption appeared after an injection which followed infiltration of the tissues with neoarsphenamine. We feel convinced that, in this case at least, the sensitization of the patient was caused by the extravasation of the drug into the tissues and also into the skin itself, which, in this manner, acted as an intradermal injection. Klauder [24] reported the case of a physician who had an intradermal injection of arsphenamine for experimental purposes. When he later came in contact with the drug during the treatment of his patients asthmatic attacks and a local eczema developed. This patient reacted positively to a patch test with a 2 per cent solution of neoarsphenamine. Klauder expressed the belief that infiltrations due to faulty technic are responsible for many cases of sensitization. He felt certain that intramuscular injections of sulpharsphenamine have likewise been responsible for a large number of reactions. Shaffer [25] suggested that small amounts of arsphenamine accidentally deposited intradermally while the needle is being withdrawn on completion of the injection may at times induce sensitization. Klauder tried to sensitize patients who were under treatment for syphilis and were receiving arsphenamine intravenously by giving them intracutaneous injections of the same drug, but failed in the attempt. Frei [26] was able to produce local sensitization by means of intradermal injections in persons who never had injections of arsphenamine, but failed

24. Klauder, J. V.: Hypersensitiveness to Local Contact with Arsphenamins Producing Chronic Eczematoid Dermatitis and Asthmatic Symptoms, Arch. Dermat. & Syph. **5**:486 (April) 1922.

25. Shaffer, L. W.: Treatment of Postarsphenamine Dermatitis, Arch. Dermat. & Syph. **29**:173 (Feb.) 1934.

26. Frei, W.: Ueber willkürliche Sensibilisierung gegen chemisch definierte Substanzen; Untersuchungen mit Neosalvarsan am Menschen, Klin. Wchnschr. **12**:539 (March 18) 1928.

to obtain any results in those who were being treated with arsphenamine at the same time. He believed that there is something in the blood of the patient who is receiving arsphenamine which prevents his sensitization. The experiments of Frei [26] and of Sulzberger [27] which were performed in Jadassohn's clinic in Breslau throw some light on the subject. They sensitized guinea-pigs by means of intradermal injections of arsphenamine. This was evidenced by means of the flare-up reaction. If the intradermal injection was followed by an intravenous injection of arsphenamine on the following day, sensitization was prevented, but if the intravenous injection was given on the fifteenth day, there was an intensification of the local reaction and, in addition, there was a generalized eruption showing that the animal had, by that time, been sensitized. They concluded that if arsphenamine is injected simultaneously or immediately after the intradermal injection, a reaction is prevented, but that if it is injected after sufficient time has elapsed for sensitivity to develop, a reaction will follow. Frei, Nathan and Munk [28] stated that a certain number of persons become sensitized after an intradermal injection of neoarsphenamine. This sensitization may be local or general. They advise against an intradermal test as it is a source of danger in further treatment with arsphenamine. According to them, the intradermal test is useful only when a patient is already known to be sensitized. In that case, a reaction to the drug in very dilute solutions should be interpreted as a danger signal, and treatment should be discontinued. On the other hand, a negative reaction to the skin test does not mean that the patient is not sensitized. For that reason, Moore and his co-workers [1] believed that skin tests are of no value in determining whether or not a person should be treated with arsphenamine. It is generally accepted that dermatitis or dermatitis exfoliativa is a positive contraindication to further treatment with arsphenamine, whereas in the exanthems the skin test has no meaning. The same may be said about the patch test. Only those patients in whom dermatitis developed as a reaction to arsphenamine gave a positive reaction to the patch test, while those with the exanthems always gave a negative reaction to the test. On the other hand, not all patients who give a positive reaction to the patch test are subject to dermatitis after injections of arsphenamine.

The question arises, What shall one do with sensitized patients? From the course of events in the case described, namely, a reaction after each injection of arsphenamine once the patient became sensitized, without any harm resulting from it, one would think that there is no objec-

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27. Sulzberger, M. B.: Hypersensitiveness to Arsphenamine in Guinea-Pigs, Arch. Dermat. & Syph. **20**:669 (Nov.) 1929.

28. Frei, Nathan and Munk, quoted by Schreiner.[29]

tion to the continuation of the treatment in this class of patients. Schreiner [29] stated that dermatitis never develops in a patient who suffers from an exanthem following the use of arsphenamine, while Kerl [30] was of the opinion that the exanthem is a contraindication to further treatment with arsphenamine. Furthermore, Schoenhoff [28] reported a case of a pityriasis rosea-like eruption after treatment with arsphenamine which was followed by a dermatitis. According to Frei, Nathan and Munk,[28] changing the arsphenamine preparation will do away with the reaction. This was not the case with our patient. The same reaction occurred after the administration of silver arsphenamine as after the administration of neoarsphenamine. The patient, however, was able to tolerate quinquivalent arsenic (tryparsamide, and acetarsone). This is thoroughly in agreement with the findings of Moore and his co-workers,[1] who stated that eleven of thirty of their patients who were sensitized to arsphenamine were able to tolerate tryparsamide.

SUMMARY

The case of a syphilitic patient is presented in whom a pityriasis rosea-like eruption developed after an injection of neoarsphenamine. This injection followed a previous infiltration due to faulty technic. The same patient had previously received a whole course of neoarsphenamine without any harmful effect. Once the patient became sensitized, the characteristic eruption appeared after every injeciton of neoarsphenamine, and likewise after the injection of silver arsphenamine, furnishing conclusive proof that we were dealing with a state of allergy due to the arsphenamine preparations. The size of the dose did not influence the severity of the reaction, but the severity of the reaction increased with every succeeding dose, no matter how small. An eruption followed the administration of even such a minute quantity of neoarsphenamine as used in the intradermal test. The reaction to the latter was positive, while that to the patch test was negative. This is characteristic for the exanthematous type of reaction. There was a complete subsidence of the reaction within a short period, and no permament injury resulted. No reaction followed the administration of quinquivalent arsenic.

CONCLUSION

There is no advantage in skin tests for sensitiveness to arsphenamine, except perhaps for experimental purposes. In the intradermal test, however, there is great danger of causing a sensitization of the patient to the drug used in the test. Likewise, faulty technic which causes

29. Schreiner, K.: Zur Pathogenese der Salvarsan-Hatschäden und deren Verhütung, Dermat. Ztschr. **67**:230 (Sept.) 1933.

30. Kerl, quoted by Schreiner.[29]

perivenous infiltration may be the cause of sensitization and therefore may be responsible for many reactions. When the patient is already sensitized, an intradermal test alone may set up a reaction. While no actual harm came to our patient from the repeated reactions, the severity of the attack increased with each succeeding injection. For that reason, we feel, contrary to some expert opinion, that we are not justified in exposing the patient to the danger of developing dermatitis exfoliativa, no matter how remote the chance is. In spite of the fact that the reaction in our case was definitely due to allergy, it was not specific for the preparation employed, for it occurred after the employment of silver arsphenamine as well as after the use of neoarsphenamine. For that reason, changing the arsphenamine preparation is not always a means of overcoming the danger of a reaction. The only arsenical preparation that these patients seem to tolerate is some form of quinquivalent arsenic.

1955 Grand Concourse.

1555 Grand Concourse.

AMERICAN DISTRIBUTION OF DEATHS FROM CANCER OF THE SKIN, MOUTH AND BREAST

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In preparing statistical material dealing with the American distribution of various diseases, I have assembled the data on the mortality due to three types of cancer for the decade 1920 to 1930: (1) cancer of the skin, (2) cancer of the mouth and (3) cancer of the breast. The statistics were originally included in the group because I assumed that the distribution would be rather uniform, but to my surprise the grouping was so distinctly regional that I believe greater attention should be devoted to the subject. The three types of cancer included in the study were selected because the diagnosis is obvious and because mistakes in diagnoses on death certificates should be far fewer for these types than for cancer of the deeper tissues.

It is well known that the incidence of cancer in general is high in the New England states, and this has been ascribed to the preponderance of an older age group on the one hand [1] and to better diagnoses on the other, but I begin to have my doubts as to whether these explanations are adequate.

CANCER OF THE SKIN

For the white race, cancer of the skin occurs in three focal regions: (1) New England, including Nova Scotia, (2) the southern states (it should be kept in mind that Texas and South Dakota are not included in the area of registration) and (3) the western coast, which shows increasing susceptibility as one proceeds southward. This is illustrated in chart 1, based on a population of 100,000.

Before I enter into an analysis of this peculiar distribution, I shall compare deaths due to two other superficial forms of cancer, namely, cancer of the mouth (chart 2) and cancer of the breast (chart 3).

CANCER OF THE MOUTH

If one examines the charts for white and colored people, one finds a distribution that is characteristic for the autonomic disturbances in general. The rate is high not only in New England but through Ontario,

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1. I have discussed the relation to age distribution in "The Patient and the Weather" (Ann Arbor, Mich., 1934, vol. 1, to be published).

and a peak is reached in Nova Scotia. Newfoundland (not shown on the map) has a rate of 3.2 per hundred thousand inhabitants. The rate remains high, and in a typical fashion includes Nebraska, Kansas and Colorado; it then promptly drops as one proceeds south, although both Louisiana and Florida show a slight increase for the white population.

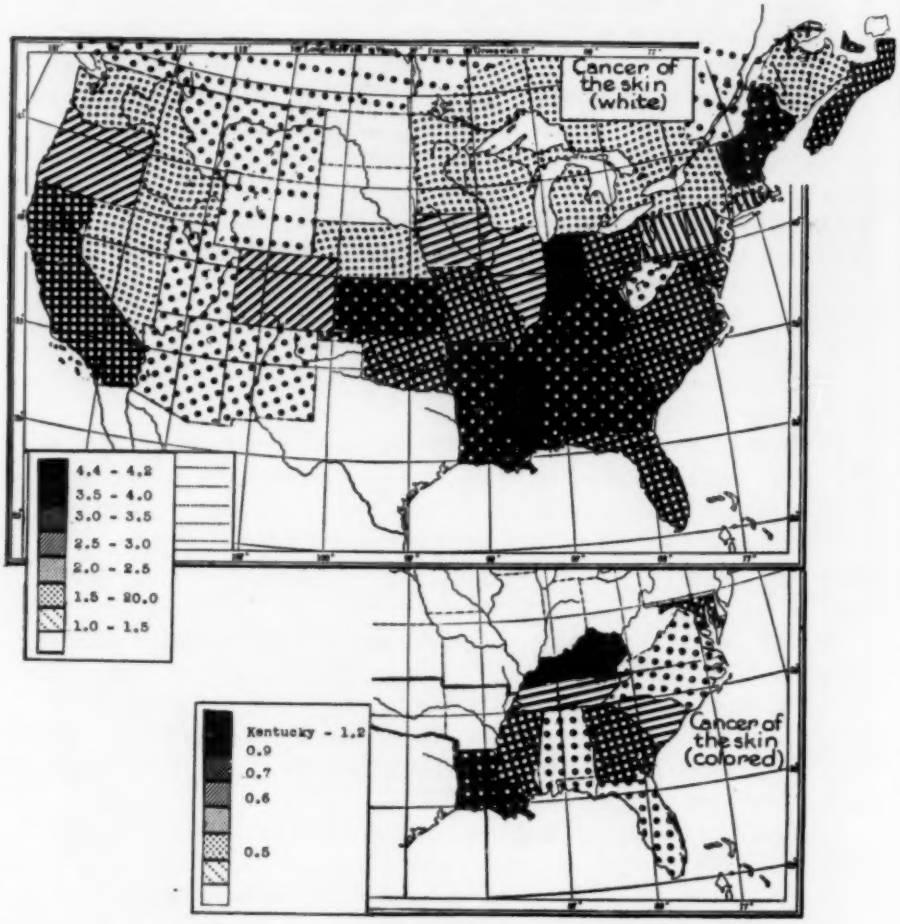

Chart 1.—Cancer of the skin in white and colored patients.

The mortality rate for the west coast is high, with that for California reaching the New England rates, but here, as in so many instances, one must keep in mind the great migration of an older age group to California from the midwestern region.

When one examines the map for the Negro mortality, one notes that the Negro dies more frequently from cancer of the mouth as he moves north, although Louisiana also shows a high mortality rate.

CANCER OF THE BREAST

With cancer of the breast the distribution is identical (the death rate is based on a female population of 100,000). As one proceeds north to Newfoundland (not shown on the map), the rate sinks to a low value of 1.8.

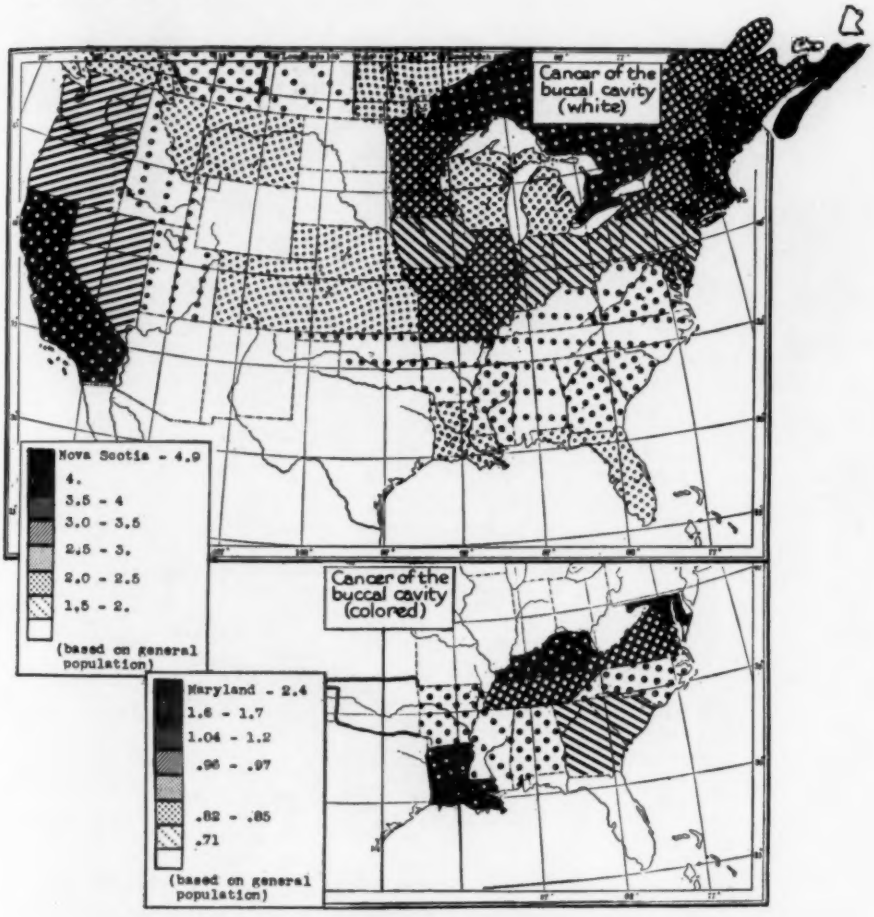

Chart 2.—Cancer of the breast in white and colored patients.

In Negroes of the states of Kentucky and Maryland cancer of the breast is more frequent. Is one to assume that this difference is due to the age distribution of the population or is one dealing with faulty diagnosis or better treatment? The treatment is probably better in the eastern states, and early diagnosis is more probable. Late diagnosis and poor treatment probably are more pronounced in the south, but the anticipated reversal of the death rate does not materialize for these two forms of cancer.

COMMENT

While cancer of the mouth and that of the breast present identical distributions, cancer of the skin offers certain definite deviations. Presumably the irritation from light plays a dominant rôle—a supposition that receives support from the fact that the Negro, whose skin is pro-

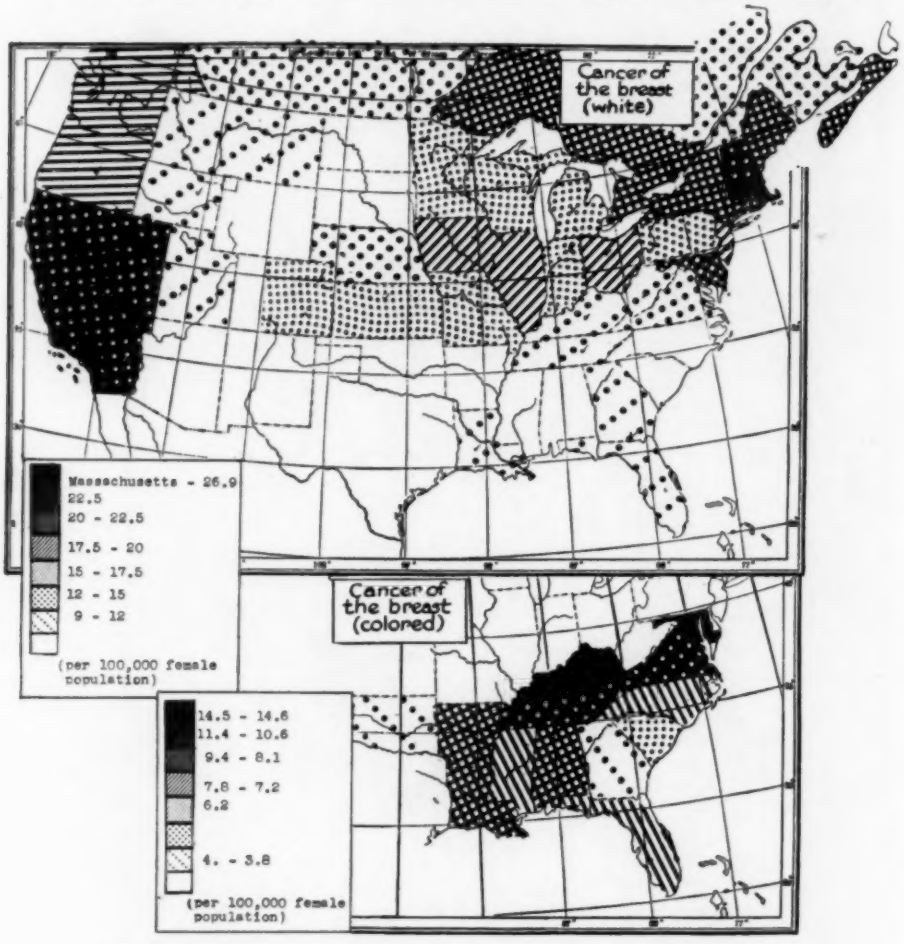

Chart 3.—Cancer of the buccal cavity in white and colored patients.

tected against ultraviolet irradiation, has less cancer of the skin in the south. But I should call attention to the fact that for the Negro Kentucky and Louisiana present the highest rates. How is one to explain these curious differences?

As a working hypothesis, one might in an arbitrary fashion postulate five components as making up the factors in an uncertain constellation, the sum total of which might bring about a transition from normalcy to malignancy. These might be classified as: *A*, age; *B*, genophasic fac-

tors (hereditary resistance and hereditary susceptibility); *C*, chronic irritation; *D*, proper ion balance, and *E*, proper endocrine balance.

Given the first three as conditionally propitious for the change of the cell from normalcy to malignancy at some particular time, it might seem that the additional factors of humoral environment must still be considered. Experimental evidence seems to be accumulating that the p_H plays some rôle (relative alkalinity), and probably the same holds true for the glands of internal secretion.

If the humoral milieu (tissue fluid) remains unchanged, or the fluctuations in the ionic and endocrine concentration swing within a small range, the probability is that the attainment of a proper constellation of ions and endocrines of just the right proportion to change the course of some cell at just the right time of its reproductive cycle will

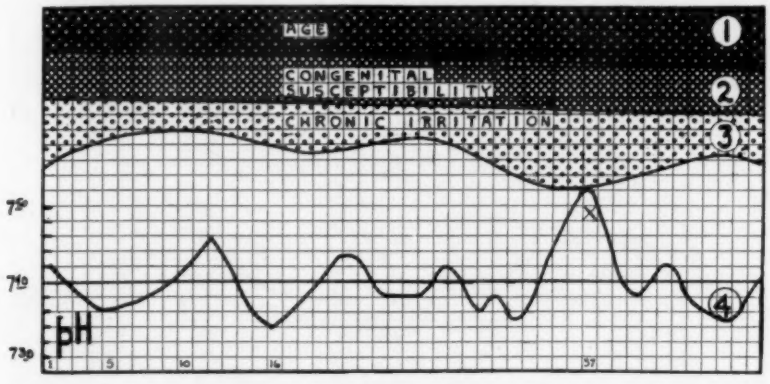

Chart 4.—Diagram illustrating the rôle of meteorological factors in the constellation of factors favoring malignancy: *1*, the gradual increase in age; *2*, a certain degree of congenital susceptibility (resistance: susceptibility); *3*, the varying degree of chronic irritation, and *4*, the fluctuating tide of the humoral milieu here illustrated in the change in the p_H curve, the changes being incidental to the meteorological adjustment.

occur less frequently than if the milieu is constantly swinging in a wide range between the two extreme poles of normalcy.

The p_H [2] may be considered for a moment. If a relatively high p_H is desirable to enhance the transition from normalcy to malignancy, (1) the pyknic person will be more liable to cancer, because he is in general more alkaline; (2) one might expect more malignancy in the south, provided meteorological quiescence, sunshine and diet raise the p_H to a sufficiently high degree, and (3) if unusual degrees of p_H are obtained, even if for only short periods of time, one might expect a proper constellation to occur more often in the cyclonic tracks, for with

2. Petersen, W. F.: Proc. Soc. Exper. Biol. & Med. **20**:1420, 1933.

the passage of each cyclone or the summation of several, one notes transient alkalotic peaks occurring as overcorrection after periods of acidity.

The same reasoning holds for the endocrine tide that is so largely involved in the mechanism of meteorological adjustment (the thyroid and suprarenal glands). With tides that have a fixed rhythm one might anticipate less influence. If it requires possibly the factors *A*, *B* and *C* and just the right constellation occurring with the combination of *D* and *E*, the more frequently the endocrine glands are stimulated and depressed, the greater is the possibility that at some time an optimal point is reached for the change from normalcy to malignancy.

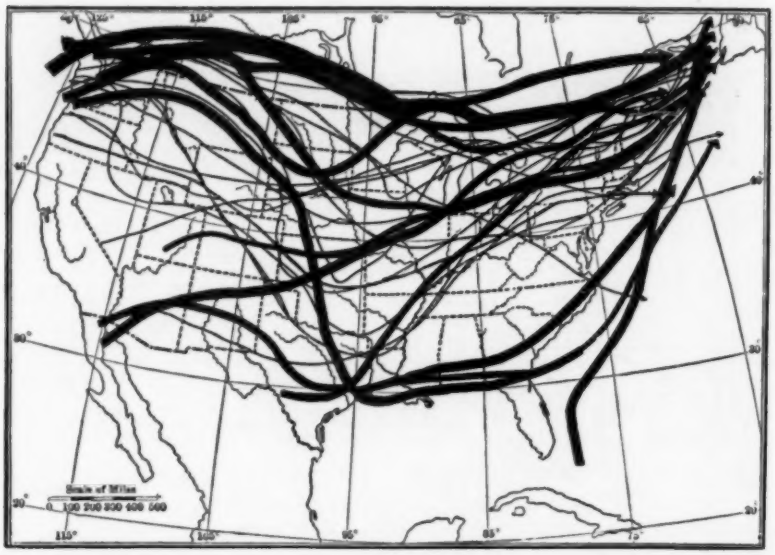

Chart 5.—Storm track map of the United States (Van Cleef, United States Weather Bureau).

Perhaps this can best be illustrated by a simple diagram. I have indicated a theoretical p_H curve (merely typical of the biologic rhythm) with a low value of 7.34 on the sixteenth day of the chart and a high value of 7.53 on the thirty-seventh day. One may assume that the high p_H affords an environment favorable for the beginning of malignancy (curve 4, chart 4). Of the innumerable other factors that might be considered, three have been indicated at the top of the graph: (1) gradually increasing age, (2) the genotypic factor, possibly a balance of inherited resistance or inherited susceptibility, and (3) chronic inflammation, varying from day to day both in the number of newly formed cells and in the degree of stimulation and degeneration.

Indicated in the diagram at *X*, a constellation would obtain when, because of the peculiar relation of age, susceptibility, irritation and proper humoral environment (in this case indicated by the p_H level), some cell might reach just the proper state for a change in its character from benignancy to malignancy.

In chart 5 I have reproduced a Van Cleef storm track map of America. This indicates the pathways along which cyclones [3] are constantly passing. Each alteration of the atmosphere brings about a distinct alteration in the blood chemistry; a synchronous and definite rhythm takes place with alternating periods of vascular spasm followed by vascular dilatation, increased p_H followed by a decline toward acidity and an increase in cholesterol followed by a diminution.

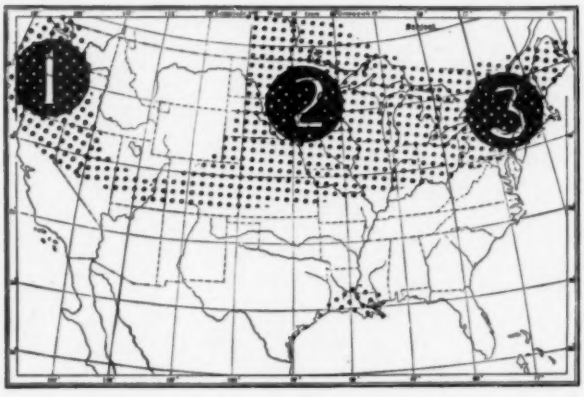

Chart 6.—Regions of maximum meteorological demand.

This will in general result in far greater instability of the blood chemistry in the region of the storm tracks than in the relatively stable southern sections. In a general way, too, the seasonal effects will be greater, and the northern population will be relatively more acid; the southern, more alkaline.

The regions of greatest autonomic demand are probably those indicated in the stippled portion of the map shown in chart 6, and reach maximal proportions in the areas 1, 2 and 3.

If one now surveys such a map as chart 2 (cancer of the mouth), one observes that, apart from California, the distribution actually follows the map of autonomic demand rather closely. The western coast forms a region of high mortality; the second transition from a low to a

3. Throughout it should be kept in mind that cyclones in the meteorological sense are not the prairie twisters but the great circulating air masses that sweep over America from west to east in counter-clockwise fashion.

high rate occurs west of the Great Lakes, and finally the New England region under the northeastern terminus of the storm tracks presents the highest rates. The South is relatively free, but the southern Negro develops more cancer of the mouth as he proceeds toward the region of the storm tracks, although Louisiana (which is also relatively unstable) presents a high rate.

For California I must assume that the migration of a large number of persons of an advanced age group who have sought to escape from the tracks of the storm region will be of importance in increasing the death rate, particularly in southern California.

For cancer of the breast practically the same distribution is found, and I believe that the same causes are effective. Chemical and endocrine (that is, autonomic) instability will more often create metabolic situations that will be favorable for the initiation of cancer.

When one now turns back to cancer of the skin, one finds fundamentally the same regions involved and the same factors responsible, but, in addition, direct irritation of the skin.

The rate at the northeastern end of the storm tracks is still high; that on the northwestern coast (Oregon) is high, and beginning in Colorado, one finds the same basic spread northeastward through Nebraska and Minnesota and again reaching a focus in New England. But while the southern region reveals less involvement from the other two types of cancer, one finds increasing rates for cancer of the skin as one passes through Oklahoma, Arkansas and Louisiana. But again the Negro shows the expected reversal. While he is, in general, immune to the effect of undue light, he is not immune to the effect of autonomic instability; as this increases, his cancer rate increases. One finds that Kentucky has the highest mortality rate for the Negro.

CONCLUSIONS

As long as one has reason to believe that the transition of cell growth from normalcy to malignancy depends on an entire series of conditioning factors, any one of which may be of paramount importance in the constellation of events, the chemical and endocrine instability that results from the severe environmental demands incident to life in the region of the storm tracks must be considered. In this note attention is called to certain peculiar features of the regional distribution of superficial cancer in America which may possibly be related to meteorological instability.

CLINICAL SPECTROSCOPY

A STUDY OF BIOPSY MATERIAL FROM PATIENTS WHO HAD RECEIVED INTRAVENOUS INJECTIONS OF SILVER ARSPHENAMINE

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AND
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When Paul Ehrlich [1] in his early experiments with dyestuff and tissue staining succeeded in simplifying the identification of the blood cells, the basis of hematology was established. The application of these principles to the microchemical reaction of tissue to dyestuff resulted in the introduction of the theory of selective affinity between chemical substances and protoplasm. Moreover, the observations from all those experiments led Ehrlich to outline his side-chain theory. In spite of the adverse criticisms of this theory, it proved to be a valuable link in the development of the science of immunity and serum reactions. After the discovery of immune bodies in syphilized blood, Ehrlich assumed that special antitoxins would not be effective in treating protozoan diseases. This conclusion initiated a series of trial and error experiments to find a *therapia sterilisans* against syphilis. As arsanilic acid was useful in the treatment of spirillar infections, compounds of this substance were varied in every conceivable way to determine what particular grouping possessed the greatest therapeutic value. The culmination of these efforts came with arsphenamine in 1910.

Working on the theory that two drugs striking together would be more effective than a single drug, Ehrlich and Karrer [2] succeeded in combining compounds containing trivalent arsenic with metallic salts. These compounds in solution do not give the reaction for metallic ions and are characterized by their great stability and intense color.

After Ehrlich's death in 1915, Kolle [3] continued this investigation. He succeeded in preparing a large series of metallic arseno-aryl deriva-

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1. Garrison, F. H.: History of Medicine, ed. 4, Philadelphia, W. B. Saunders Company, 1929, p. 709.

2. Ehrlich, Paul: Brit. M. J. **2**:353, 1913. Ehrlich, Paul, and Karrer, P.: Ber. d. deutsch. chem. Gesellsch. **48**:1634, 1915.

3. Kolle, W., and Ritz, H.: Experimentelle Untersuchungen über die Wirkung des Silbers und seiner Verbindungen auf die Kaninchensyphilis mit besonderer Berücksichtigung des Silbersalvarsans, Deutsche med. Wchnschr. **45**:481 (May 1) 1919.

tives. From this group of salts the compounds of only two metals, gold and silver, appeared to have the desired effect on the spirochetes. Parallel experiments proved that the silver salt was superior to the gold salt in its therapeutic value and, furthermore, had a lower toxicity. The effectiveness of the silver salt was attributed to the presence of two chemotherapeutic agents, arsenic and silver, and possibly to the catalytic action of silver on the arsphenamine molecule.

Myers [4] described silver arsphenamine as the completely alkalinized monosilver salt of arsphenamine. It is a brownish-black powder, unstable in moist air and in moist air containing carbon dioxide. The

TABLE 1.—*Reported Cases of Argyria After Silver Arsphenamine*

	Case	Age	Date of Injection	No. of Injections	Total Dosage, Gm.	Appearance of Argyria
Spiegel, L.: Arch. Dermat. & Syph. **23**: 266 (Feb.) 1931	1	23	3/25/26 10/31/28	28	5.6	August 1928
			1/ 4/29 8/11/29	10	2.0	May 1929 (quite evident)
					7.6	
	2	54	5/25/27 12/28/28	15	2.9	June 1929
			9/ 5/29 11/10/29	16	1.2	September 1929 (more marked)
					4.1	
	3	49	Nov. 1924 Nov. 1926	34	10.2	November 1929
Becker, S. W., and Ritchie, E. B.: J. A. M. A. **97**: 389 (Aug. 8) 1931	1	53	Four years	60	16.5	Nov. 11, 1930
	2	65	May 1924 July 1926	57	17.1	Nov. 11, 1930
Sioli, F.: Arch. f. Psychiat. **68**: 321, 1923	1	37	1/31/19 8/29/21		20.0	July 10, 1922 (slight discoloration noticed)
	2	..	7/10/22 10/23/22	..	2.5	March 1923 (discoloration very distinct)
					22.5	

slight changes in color are due to the state of the physical aggregation of the particles. (The importance of this property of the drug will be brought out later in this paper.) It is readily soluble in cold water, giving a slightly alkaline reaction and a sulphonated bitumen-brown solution. It contains approximately 20 per cent arsenic and 14 per cent silver. The drug was first used clinically in March 1918.

The widespread use of silver arsphenamine indicates a general belief that only a remote possibility of resulting development of argyria exists. However, a number of cases of argyria have been reported from this cause. Table 1 gives the dosage and the time of appearance of argyria.

Since a number of cases of argyria have developed through the use of silver arsphenamine, this investigation was started to determine the

4. Myers, C. N.: Silver Salvarsan, Qualitative and Quantitative Studies, Am. J. Syph. **6**:1, 1922.

retention of this drug by connective tissue or cutis. In work reported in an earlier publication [5] a spectographic method of analysis had been successfully used in the detection of gold in biopsy specimens from patients receiving gold sodium thiosulphate for lupus erythematosus. The procedure described in that paper has been applied to the detection of silver in biopsy specimens from patients receiving silver arsphenamine. Table 2 shows the dosages given patients. As before, the biopsy specimens were taken with a 3/16 inch (0.47 cm.) punch and each specimen weighed about 0.025 Gm.

TABLE 2.—*Dosage of Silver Arsphenamine Given Patients from Whom Biopsy Specimens Were Taken*

Patient	Number	Age	Number of Injections	Dates of Injections	Date of Biopsy	Site of Biopsy Specimen	Total Dosage, Gm.
A	1	42	3	5/ 6/33 5/20/33	5/27/33	Right forearm	0.225
B	2	30	5	5/ 1/33 6/ 7/33	6/27/33	Right arm	0.50
FC	3	49	3	5/ 3/33 5/31/33	6/ 6/33	Lumbar region	0.55
C	4	36	4	9/23/32 11/ 1/32	6/ 6/33	Right thigh	0.65
D	5	50	6	4/25/33 6/ 1/33	6/ 3/33	Right arm	0.75
E	6	31	4	5/ 8/33 5/31/33	6/ 7/33	Right side of chest	0.80
F	7	31	7	4/11/33 5/25/33	6/ 1/33	Right thigh	0.90
G	8	31	8	12/26/32 2/20/33	6/ 6/33	Left arm	1.45
Hu	9	48	12	6/13/32 12/28/32	6/13/33	Left shoulder	1.80
Go	10	36	11	2/24/33 6/ 7/33	6/ 6/33	Left flank	2.05
H	11	39	25	10/28/30 8/29/31	6/ 6/33	Left forearm	4.55
Gr	12	45	40	4/ 8/32 6/15/33	6/12/33	Abdomen	4.90
Hl	13	36	39	5/17/29 3/13/31	6/12/33	Right side of chest	5.775

METHOD

To obtain a general idea of the amount of silver present in the biopsy specimens, a series of standard solutions of silver nitrate of different concentrations were prepared: One drop of solution 1 contained 0.0000001 Gm. of silver; 1 drop of solution 2 contained 0.000001 Gm. of silver, and 1 drop of solution 3 contained 0.00001 Gm. of silver. The spectra of the biopsy specimens from the patients listed in table 2 and of the standard solutions were photographed on the same plate under identical conditions. For taking spectrograms of the standard solutions 1 drop of each solution was used.

5. Gaul, L. E., and Staud, A. H.: Clinical Spectroscopy: A Study of Biopsy Material Taken from Patients Receiving Gold Sodium Thiosulphate, Arch. Dermat. & Syph. **28**:790 (Dec.) 1933.

From an examination of the spectrograms of the standard solutions as shown on the plate, it is obvious that as the concentration of the silver is increased, the density of the silver lines is increased. If an unknown sample contains an amount of silver within the concentration range of the standard solutions (from 0.0001 to 0.0000001 Gm.) and if the spectra of the unknown solution and the standard solutions are photographed on the same plate under identical conditions, the amount of silver in the unknown solution can readily be estimated by comparing the density of the silver lines given by the unknown solutions with that of those given by the standard solutions. On this characteristic are based the principles of quantitative spectrochemical analysis.

For comparing the densities of spectral lines, a Moll recording microphotometer was used. A microphotometer is primarily an instrument for investigating photographed spectra. The spectrogram is fixed on a plate holder. A beam of light passes through the negative on its way to a thermopile connected to a moving coil galvanometer, and the deflections of the galvanometer are photographically recorded on a sheet of bromide paper stretched round a drum. By moving the plate holder

TABLE 3.—*Amount of Silver Found in Biopsy Specimens*

Patient	Number	Total Dosage of Silver Arsphenamine, Gm.	Silver in Biopsy Specimen, Gm.
A	1	0.225	Slightly more than silver content in normal skin
B	2	0.50	
FC	3	0.55	
C	4	0.65	
D	5	0.75	
E	6	0.80	
F	7	0.90	
G	8	1.45	0.000000088
Hu	9	1.80	0.000000092
Go	10	2.05	0.000000095
H	11	4.55	0.00000047
Gr	12	4.90	0.00000055
Hi	13	5.775	0.00000071

and at the same time rotating the drum, a record is made showing all the details of the spectrum under examination. Since the deflections of the galvanometer are governed by the amount of light which passes through the line being measured, and the amount of light passing through the line is proportional to its density, a comparison of the densities of the lines can be made from this photometric record produced by the microphotometer.

When the photometric curves for the silver line 3,280.67 angstrom units in the spectrograms of the standard solutions and the biopsy specimens had been completed, the conversion of these density measurements to the amount of silver present gave the results shown in table 3.

Since silver has been shown to be a normal constituent of the cutis or connective tissue, a series of biopsy specimens from normal persons ranging in age from 6 months to 65 years was tested for silver. The procedure outlined gave the average result for a series of twenty-five biopsy specimens of 0.000000075 Gm. of silver in a sample of skin weighing 0.025 Gm.

COMMENT

In a true solution, such as saline solution, the molecules of sodium chloride are in equilibrium with the sodium and chloride ions. Solutions

of this type readily diffuse through cell membranes. Silver arsphenamine, however, when dissolved in water forms a colloidal solution. The solvent is the continuous phase and the silver arsphenamine is the dispersed phase. Colloidal particles do not pass through cell membranes. Thus, the physical and chemical properties of the solution to be injected determine the extent of the physiologic reaction on the part of the body. This physiologic reaction is a response of the differentiated and the undifferentiated connective tissue.

The adult connective tissue structures develop from primitive mesenchyme or mesoderm. Through a process of differentiation the skeletal, muscular and fascial systems as well as the organs of excretion and the internal genitals are formed. It further gives rise to the entire hematopoietic system. Thus, the derivatives of mesoderm form a vast complex separating ectodermic and entodermic structures. The circulating blood and the loose areolar tissue surrounding the capillary system are not separable. A cellular response in one produces a response in the other. The ultimate fate of any substance entering this system through the gastro-intestinal tract, through the ectoderm or by way of the veins is determined by the reaction of the connective tissue. When particulate matter (referring to silver arsphenamine) enters the blood stream, the body answers by an "activation of the mesenchyme." This is a response of leukocytes or differentiated connective tissue, and a response of the cellular elements of the areolar tissue surrounding the capillaries which remains undifferentiated throughout the life of the individual. It is this response that determines the distribution, localization and excretion of the drug. In the case of particulate matter, such as silver arsphenamine, the retention by connective tissue, as well as the distribution and excretion, is brought about by the cellular elements engulfing the particles, by phagocytosis.

CONCLUSIONS

1. A biospectrometric [6] test is applicable for the detection of metallic constiuents in normal and pathologic tissue.

2. The amount of skin required for the test does not inconvenience the patient or leave a noticeable scar.

3. The spectrochemical method of analysis gives not only qualitative but also quantitative results.

4. Thirteen biopsy specimens were analyzed.

5. A total dosage of silver arsphenamine varying from 0.225 Gm. to 0.9 Gm. gives a silver content slightly greater than that found in normal skin.

6. The word biospectrometric specifies a quantitative spectrographic analysis for the metallic constituents in differentiated and undifferentiated mesoderm, obtained by taking a dermal biopsy specimen with a 3/16 inch (0.47 cm.) punch, the specimen weighing approximately 0.025 Gm.

6. The deposition of the silver is uniform throughout the cutis (table 2, column 6).

7. The retention of silver by connective tissue or cutis is cumulative and is directly proportional to the total dosage received (table 3).

8. Although biopsy specimens were taken in the cases of Hu, H, and Hi six months, two years and two and a half years, respectively, after the last injection, the quantity of silver present remained proportional to the total dosage.

NOTE.—Since the submission of this report for publication a biospectrometric analysis of eight additional cases confirmed the supposition that the quantity of silver retained by connective tissue or cutis is directly proportional to the total dosage of silver arsphenamine administered. To date, fifteen cases of argyria following silver arsphenamine therapy have been observed and reported. In a report to be published in *The Journal of the American Medical Association,*[7] it was established that argyrosis becomes clinically apparent after a retention of silver approximating an equivalent of 8 Gm. of silver arsphenamine.

7. Gaul, L. E., and Staud, A. H.: Clinical Spectroscopy: Sixty Cases of Generalized Argyrosis Following Organic and Colloidal Silver Medication Including a Biospectrometric Analysis of Ten Cases, J. A. M. A., to be published.

Correspondence

DERMATOLOGIC EXAMINATION: A CANDIDATE'S IMPRESSION

To the Editor:—Now that 1933 examinations for the American Board of Dermatology are over, one looks back on certain phases of them that might be improved for the benefit of future candidates.

I filed my application by September 1, as the written examination was scheduled for October 28, but I did not receive a notification to appear until nine days prior to the date for the examination. If notification is given four or five weeks in advance a candidate can adjust his program to provide for study and review. It is difficult for him to add extra studies to his routine until he is definitely listed for examination.

Three hours (from 2 to 5 p. m.) were allotted for the written examination. When I handed in my paper it was 6:20 p. m., and five or six of the eleven candidates were still working over their problems. My thought was, "The examination is too extensive for the time allowed." A physician taking the examinations is under tension and has been for many days. At the end of three or four hours of intense concentration he is tired, and a free flow of thought is impossible. A more equitable time schedule should be granted for the examinations.

Many of the questions which were submitted called for differential diagnoses, which in a written examination are time-consuming, as prolonged thought is necessary. A simpler method, producing equally effective results, should be devised. The questions were fair, but they required comprehensive answers. Many candidates are not gifted with the ability to tell a great deal in a few expressive, "highlight" words. They grope a long time before the proper expression presents itself. Problems in differential diagnosis may well be reserved for the clinical examinations.

The oral examination took place on December 15, two months after the written examination. Notification for the oral examination was received eleven days before the scheduled date. During this interval the candidate was uncertain as to whether he was to be admitted. He had to assume that he had successfully passed the written tests before he could start with enthusiasm to prepare for the oral examination. It is difficult to concentrate during uncertainty.

The oral or clinical test in December was more satisfactory. In this type of examination more ground is covered, and mistakes are avoided that on paper would stand as a permanent record. The oral test gives more opportunity for development of thought; it provides a larger degree of clarity and eliminates the possibility of misunderstanding. The examiner can be certain that the applicant knows what he is talking about. The written examination, on the contrary, in a sense deprives the applicant of the opportunity to impress the examiner. The personal contact of the conversational method allows a freedom of action that permits the examiner to state a question in three or four different ways, which makes it probable that he will draw out the full knowledge of the applicant. It is fundamentally fair to the candidate and the board of examiners.

In an examination of this kind, which is national in scope, it is of interest to learn in what branch of the subject the candidates are weak. I asked a number of candidates, and practically all of them said that they found syphilis of the

viscera and central nervous system the most difficult. This may be due to insufficient instruction in this subject by the graduate schools. It is more likely due to the fact that the average dermatologist does not see enough cases of this sort to hold his interest and compel him to study the subject extensively. On the subject of the cutaneous manifestations of syphilis, which the physician sees often, the answers were more satisfactory. The majority of the work of dermatologists outside of large clinics is in dermatology proper, and the amount of syphilis is proportionately small; yet it is essential that the dermatologist know the manifestations of syphilis in the skin.

The pathologic examination consisted in the use of slides under the microscope for the purpose of diagnosing and identifying pathologic changes in the tissues. The slides were elemental; nothing was shown except what a qualified dermatologist should be able to identify.

The general pathologist knows relatively little about pathologic conditions of the skin and readily admits it. It is therefore essential that the dermatologist know something of this subject. I feel that a postgraduate course in dermatology should include pathology. The graduate school ought to provide a set of pathologic slides for the students' constant reference. It is almost impossible to obtain pathologic slides except from large clinics.

For the guidance of those who contemplate taking the examinations, I should say that they cover practically every aspect of rare and common cutaneous and syphilitic conditions.

I have asked myself, "Is an examination of this sort worth taking, with all the extra work and anxiety which are entailed?" The answer is emphatically "yes." The examination puts the student on his toes and brings back many dermatologic details long forgotten. Also, there is the satisfaction of accomplishment and progress.

RAYMOND V. QUINLAN, M.D., Meriden, Conn.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

COD LIVER OIL SENSITIVITY IN CHILDREN. R. M. BALYEAT and RALPH BOWEN, Am. J. Dis. Child. **47**:529 (March) 1934.

In two of four allergic children who were sensitive to cod liver oil, urticaria was produced by the addition of cod liver oil to the diet; in one, diarrhea, and in the fourth, eczema. The children tolerated satisfactorily carotene concentrate fortified with vitamin D.

TUBERCULIN OINTMENT PATCH TEST. ERNST WOLFF, Am. J. Dis. Child. **47**:764 (April) 1934.

While the intracutaneous tuberculin test is regarded as the most sensitive procedure now available, there are many difficulties which preclude its general use. To overcome these difficulties, Wolff used a tuberculin ointment which contained highly concentrated tuberculin and killed tubercle bacilli.

Patch tests were made with this tuberculin ointment, using the ointment base as a control. The patches were left on for forty-eight hours, and the results were then read. Positive reactions showed redness, papules, induration and a yellowish-brown pigmentation. The results of the tuberculin patch tests were in agreement with those of the intracutaneous tests in 95.8 per cent of a group of 190 patients. Thus far the author has not encountered general or focal reactions.

ANDERSON, Los Angeles.

A STUDY OF JAUNDICE IN SYPHILIS. UDO J. WILE and W. M. SAMS, Am. J. M. Sc. **187**:297 (March) 1934.

From the incidence of jaundice following the use of the arsenobenzenes, Wile and Sams believe that the drugs possess a high degree of hepatotoxicity, especially in view of the low incidence of jaundice in untreated syphilis. They do not concur with Milian in believing posttherapeutic jaundice to be a hepatorecurrence. They were able to differentiate delayed posttherapeutic jaundice and catarrhal jaundice only by the history.

About 60 per cent of their cases of posttherapeutic jaundice as well as about 50 per cent of the catarrhal cases studied occurred during a three year period. There may be a relationship between these two types.

In two fatal cases with a pathologic diagnosis of acute yellow atrophy all indications pointed to severe intoxication and destruction of liver substance. Such hepatic accidents will continue to be complications of arsenical treatment of syphilis until the drugs are rendered less hepatotoxic and more accurate means are employed to determine liver function and susceptibility.

JAMIESON, Detroit.

THE PHYSIOLOGY OF ELECTROPYREXIA. C. A. NEYMANN and S. L. OSBORNE, Am. J. Syph. **18**:28 (Jan.) 1934.

Electropyrexia is a mode of therapy becoming popular, especially in the treatment of dementia paralytica. Thus far, however, attempts at treating primary syphilis by this method have been unsuccessful. As a basis for a sounder understanding of the subject, research was undertaken on the mechanism of fever with especial emphasis on the variations in temperature of different parts of the body.

Machines for producing fever depend on the application of external heat and of penetrating heat. Among the conclusions reached are these: A heat-insulating bag will raise the rectal or axillary temperature almost 5 F. Electric blankets produce a slow rise in temperature. Whenever external heat is applied, the surface temperature of the body rises quickly, while for a time the internal temperature remains relatively cooler. Blanket treatments appear to be much more exhausting and to result in less perspiration than diathermic or radiothermic therapy. There is a definite relation between the intake of water and loss of water by perspiration with a consequent loss of weight after every treatment. For each rise in temperature of 1 F. the basal metabolic rate shows an average rise of 7 per cent. Owing to a concentration of body liquids, there is an increase of red and white blood corpuscles and hemoglobin and of the nonprotein nitrogen and uric acid content of the blood. There is a rise in systolic blood pressure and drop in diastolic pressure during treatment. While scopolamine hydrobromide inhibits perspiration and causes the axillary temperature to soar above the rectal temperature and often causes violent delirium, morphine does not. The administration of sweat-inhibiting drugs during treatment is contraindicated.

By means of specially contrived instruments for recording temperatures, it was found that the temperatures of the depths of the body were 2 F. higher than the subcutaneous temperatures of the thorax and abdomen. More distally, the subcutaneous temperature becomes less. This ratio is maintained with penetrating heat, but with external heat the ratio is gradually reversed. It is possible to raise the internal temperature of the human body, including that of the liver, cisterna magna, spinal canal, rectum and colon, to above 42 C. (107.6 F.) for periods exceeding two hours and often extending to four hours. Possibly, the difference in the temperature of the depths of the body as compared to subcutaneous temperature explains the seeming contradiction between the excellent results obtained in treating patients with neurosyphilis and the poor results recorded in the treatment of patients with primary syphilis.

SINGLE CELL INOCULATIONS WITH TREPONEMA PALLIDUM. C. S. THOMAS and H. J. MORGAN, J. Exper. Med. **59**:297 (March 1) 1934.

Sixteen rabbits were inoculated with a single, morphologically typical, motile Spirochaeta pallida; one was inoculated with two organisms, and another with six. Infection failed to follow any of the inoculations, while control animals inoculated with the usual quantity of the same but undiluted virus all presented typical lesions of experimental syphilis.

Further experiments and tissue transfers to a second and third series of rabbits failed to demonstrate the presence of the organism.

The authors conclude that negative tissue transfers neither preclude the presence of Spirochaeta pallida nor indicate freedom from syphilis in the source.

JAMIESON, Detroit.

ARSENOXIDE IN RELATION TO THE TOXICITY AND THERAPEUTIC ACTIVITY OF ARSPHENAMINE AND NEOARSPHENAMINE. J. F. SCHAMBERG, J. A. KOLMER and H. BROWN, Am. J. Syph. **18**:37 (Jan.) 1934.

The napthoquinone color test (Rosenthal) for arsenoxide, an oxidation product of arsphenamine, was found to be highly sensitive for the detection of this substance in solutions of arsphenamine and neoarsphenamine aerated with oxygen or exposed to the air. The test is much less sensitive for the detection of arsenoxide in the tissues after the administration of the arsphenamines. Freshly prepared solutions of arsphenamine and neoarsphenamine do not contain detectable amounts of arsenoxide by this test. The toxicity of arsphenamine was about doubled when approximately 34 per cent of arsphenamine in alkalinized solution was oxidized to arsenoxide with oxygen. Similar tests performed with neoarsphenamine did not correspond nearly so closely with the toxicity tests as observed with solutions of

arsphenamine, suggesting that with neoarsphenamine, at least, arsenoxide is but one factor in toxicity. Tests for arsenoxide in commercial samples of neoarsphenamine will not prove of any practical value in determining the toxicity of these compounds.

The presence of from 34 to 36 per cent arsenoxide in solutions of arsphenamine and neoarsphenamine hastened spirocheticidal effects in rabbits with acute testicular syphilis and likewise reduced the minimal curative dose of each compound about one-half.

REUTER, Milwaukee.

THE RELATION OF ALLERGY TO IMMUNITY IN TUBERCULOSIS. HERBERT ROTHSCHILD, JONAS S. FRIEDENWALD and CLARENCE BERNSTEIN, Bull. Johns Hopkins Hosp. **54**:232 (April) 1934.

In an extensive experimental investigation on guinea-pigs the authors show that immunity to tuberculosis is not impaired by the abolition of allergy. These findings show that allergy is not necessary for the operation of immunity. The work was obviously stimulated by Rich, who has recently and repeatedly demonstrated in a variety of different infections that allergic inflammation is not necessary either for the inhibition of spread or for the successful destruction of bacteria in the immune body. The article should be read in toto by all dermatologists who use tuberculin or who are interested in allergic phenomena.

ANDERSON, Los Angeles.

PRIMARY CUTANEOUS ACTINOMYCOSIS: WITH A NOTE ON THE BACILLUS ACTINOMYCETEM COMITANS. R. KLABER, Brit. J. Dermat. **46**:12 (Jan.) 1934.

The author reports the case of a man, aged 69, who injured the back of his left hand and subsequently had a diffuse, ill defined, pigmented, rather "boggy" induration containing a few scattered pustules. The condition spread over the fingers and around the wrist. Swabs taken from the sterilized, scarified, proximal-growing edge, after scraping of the affected area, and sown directly on blood agar plates yielded pure cultures of Bacillus actinomycetum-comitans, a very small gram-negative coccobacillus closely resembling morphologically the Brucella group. Minute nodules of actinomycetes were found in serial sections, and later a single pinpoint nodule of the ray fungus was recovered from an abscess. The history, literature and diagnosis of primary actinomycosis are reviewed. The diagnosis and biologic significance of B. actinomycetum-comitans are considered. Two clinical photographs and a photomicrograph accompany the article.

TREATMENT OF SUPERFICIAL STAPHYLOCOCCAL INFECTION BY TOXOID. J. I. CONNOR and MAROT MCKIE, Brit. J. Dermat. **46**:20 (Jan.) 1934.

The authors were able to establish in rabbits complete immunity to staphylococcic toxin and to massive doses of living toxigenic staphylococci introduced intravenously. This immunity was accompanied by a marked rise in the antitoxin content of the serums of the animals. An examination of the serums of 120 patients suffering from superficial staphylococcic infections, such as furunculosis and sycosis barbae, and a comparison with normal serums show that this type of infection is accompanied by a slight but definite rise in the antitoxin content. The work suggested that injections of toxoid in man might be of value in the treatment of such infections in which the immunity response was inadequate. The results in the patients treated are presented in two tables. Patients with furunculosis usually responded to from six to eight injections of toxoid. Of the eighteen patients with sycosis treated, in ten the condition cleared up completely. Four patients reached a stage in which pustules appeared each week in spite of the fact that their serum had a high content of antitoxin. The toxin was prepared by the method of Burnet and was detoxicated by incubation for five days at 37 C., after the addition of 0.2 per cent formaldehyde, and then tested for toxicity by injection into a vein of the ear of a rabbit. The recent literature pertaining to the subject is reviewed.

WIEN, Chicago.

OBSERVATIONS ON FILARIASIS IN SOME AREAS IN INDIA: X. GWALIOR STATE AREA. V. T. KORKE, Indian J. M. Research **21**:569 (Jan.) 1934.

The incidence of filariasis was found to decrease in the higher altitudes. A comparatively high incidence was found between 500 and 1,000 feet. At this level the age group of from 20 to 30 years and upward showed the highest incidence. In the 60 to 70 year group the incidence was between 22 and 33 per cent.

The area surveyed is markedly different in physical, climatic and crop conditions from other areas in India in which there is a similar incidence of the disease.

JAMIESON, Detroit.

THE CUTANEOUS CIRCULATION IN THE LIGHT OF HIGH MAGNIFICATION CAPILLAROSCOPY. E. G. SCOLARI, Gior. ital. di dermat. e sif. **74**:1117 (Oct.) 1933.

The author presents a complete and well prepared résumé of the subject of capillaroscopy. For those interested in the physiology of the circulation of the skin this is an invaluable contribution. The high magnification capillaroscope of Vonwiller was used by the author in his researches on the action on the vessels of the cutaneous papillae of epinephrine and a preparation from the posterior lobe of the pituitary gland. Under the action of epinephrine the capillaries of the papillae do not contract but remain open and filled with blood plasma; erythrocytes are absent. The same phenomenon is observed under the influence of the preparation from the posterior lobe of the pituitary gland. This stasis of blood plasma in the capillaries is best studied under high magnification in the posterior portion of the nail wall. The phenomenon is supposed to be a colloidochemical process due to the disturbance of the plasmatic equilibrium, resulting in alteration of the normal relations between the red cells and the plasma and of the quantitative proportion of these two fundamental elements of the blood. The author considers at length the question of capillary changes in angioneurosis and in Raynaud's disease.

PARDO-CASTELLO, Havana, Cuba.

CARCINOMATOUS METASTASES IN THE SKIN RESEMBLING HEMOLYMPHANGIOMA. W. NIX, Dermat. Wchnschr. **97**:1551 (Nov. 4) 1933.

The author reviews the subject of secondary cutaneous carcinomatosis, pointing out the various forms that this condition may assume. A case is described in which the cutaneous metastases took the form of hemolymphangioma.

DEMONSTRATION OF BACILLUS CRASSUS IN LESIONS IN THE MOUTH IN ULCUS VULVAE ACUTUM. A. PHILADELPHY, Dermat. Wchnschr. **97**:1556 (Nov. 4) 1933.

A patient with lesions of ulcus vulvae acutum on the labia presented aphthous lesions on the mucous membrane of the mouth. Bacillus crassus was demonstrated from both the oral and genital lesions by smears and by cultures.

EFFICIENCY OF THE GOLD SOL AND MASTIC TESTS IN SYPHILITIC CONDITIONS. ALWIN HILDEBRANDT, Dermat. Wchnschr. **97**:1558 (Nov. 4) 1933.

The author reviews his experiences with the gold sol and mastic tests of the spinal fluid. He concludes that these tests are of considerable value in checking the progress of treatment but that the results are not to be considered as final in differentiating the various types of syphilis of the central nervous system. The reactions must always be critically interpreted in connection with the other clincal findings.

COMBINED TREATMENT OF LUPUS VULGARIS WITH GRENZ RAYS AND DIET. H. T. SCHREUS and W. ENGELHARDT, Dermat. Wchnschr. **97**:1595 (Nov. 11) 1933.

Long-wave roentgen irradiation is the treatment of choice for lupus vulgaris. The individual dose is never over 1,500 roentgens and is given at intervals of from ten days to three weeks. An area of normal skin extending from 0.5 to 1 cm. from the pathologic area is irradiated along with it. Each irradiation should cause erythema, starting from three to eight days after treatment. The total dose usually amounts to from 5,000 to 6,000 roentgens. The results are attained more rapidly and less radiation is required if the treatment is combined with a salt-free diet. No damage has been observed to result from this treatment.

THE DEMONSTRATION OF CHOLESTEROL. H. MÜHLPFORDT, Dermat. Wchnschr. **97**:1651 (Nov. 25) 1933.

Most tests for cholesterol have the objection that they also react to lecithin. The author has found the following test highly specific: 2 cc. of a chloroform solution of cholesterol plus 3 drops of a 1 per cent chloroform solution of victoria blue 4R plus 3 drops of a 1 per cent methyl alcohol solution of digitonin plus 5 cc. of a saturated solution of trinitrophenol. The immediate development of "snow crystals" indicates the presence of cholesterol.

HISTOLOGIC DEMONSTRATION OF SCHIZOSACCHAROMYCES HOMINIS IN THE UMBILICAL CORD. T. BENEDEK, Dermat. Wchnschr. **97**:1653 (Nov. 25) 1933.

A special histologic technic is detailed by means of which it was possible to demonstrate Schizosaccharomyces hominis in both the veins and the arteries of the umbilical cord in a number of instances. This indicates that the organism may go from mother to fetus and from fetus to mother. Photomicrographs of the organism are shown.

RELATIONSHIP OF GLOSSITIS MARGINATA TO LYMPHOGRANULOMATOSIS INGUINALIS. WALDEMAR E. COUTTS, Dermat. Wchnschr. **97**:1664 (Nov. 25) 1933.

Twelve patients presented a condition of the tongue in which the borders were swollen and infiltrated. In some instances opaque bullae occurred. The cervical lymph nodes were enlarged. There was no pain, but speech and eating were somewhat hindered. Antisyphilitic therapy was unavailing. In all twelve cases the Frei test was positive. This condition is exceedingly resistant to therapy.

FLUORESCENCE OF THE ELASTIC FIBERS OF THE SKIN. S. BOMMER, Dermat. Ztschr. **67**:319 (Oct.) 1933.

By means of a microscope equipped with lenses relatively transparent to ultraviolet rays and with the water-cooled mercury vapor arc lamp as a source of radiation, the author was able to demonstrate that the elastic fibers of the skin fluoresce. They appear light blue or blue white and can be photographed. Frozen sections of fresh or formaldehyde-fixed tissue may be embedded in water or in glycerin. One of the explanations for the fluorescence of these fibers is the high content of silicic acid.

SKIN DISEASES DUE TO PLANTS WITH PARTICULAR REFERENCE TO MEADOW DERMATITIS (WIESENDERMATITIS). JOSEF SCHLAMMADINGER, Dermat. Ztschr. **67**:324 (Oct.) 1933.

A case of dermatitis due to asters and another due to chrysanthemums are described. In each instance the plant responsible was identified by patch tests.

A case of a bullous and vesicular eruption on the knees, legs, ankles and feet is described. The eruption started three or four hours after the patient had

worked barefoot in a field. In nine men vesicular and bullous eruptions developed on the trunk a few hours after they lay down to rest in a field while naked from the waist up.

These ten cases are considered examples of meadow dermatitis (*Wiesendermatitis*). Marked persistent pigmentation followed the dermatitis. Patch tests with various weeds found in the locality failed to identify the irritant. The author believes the condition to be a toxicodermia rather than a hypersensitivity.

ETIOLOGY, THERAPY AND PROPHYLAXIS OF ARSPHENAMINE ERUPTIONS. PAUL FASAL, Dermat. Ztschr. **68**:1 (Nov.) 1933.

An intensive study is presented of 125 cases of arsphenamine eruptions occurring in the course of five years. These comprised 68 cases of "ten day erythema," 39 of "early dermatitis" (occurring after the fifth or sixth injection) and 18 of "late dermatitis" (occurring after the end of the course of treatment). Patients with late and congenital syphilis were rarely affected. All of the 7 fatal cases were in outpatients. Paravenous injection might explain the sensitization in 4 cases. Intracutaneous and patch tests appeared to be of no value, and passive transfer tests failed. Desensitization could not be produced by increasing doses. The most satisfactory therapeutic procedure was the administration of sodium thiosulphate intravenously and by enema. In severe cases a milk diet followed by a salt-poor diet was of value. The use of sodium thiosulphate or dextrose solution as a vehicle for the arsphenamine did not alter the incidence of dermatitis though it decreased the number of angioneurotic reactions. Further treatment with a different member of the arsphenamine group may be safely carried out on some of the patients with ten day erythema, but it should be carefully controlled. Further treatment of those who have had early or late dermatitis is not successful.

CLINICAL AND CULTURAL OBSERVATIONS OF ACHORION QUINCKEANUM. K. BEINTEMA, Dermat. Ztschr. **68**:21 (Nov.) 1933.

In the clinic in Groningen, the Netherlands, an average of one hundred cases of infection with Achorion Schoenleinii are seen each year. During the course of six years seven cases of infection with Achorion quinckeanum were observed. Two of these are described, with the cultural findings.

TREATMENT OF RECURRING HERPES. H. HRUSZEK, Dermat. Ztschr. **68**:27 (Nov.) 1933.

The author reports encouraging results in the treatment of recurring herpes genitalis by means of serial autoinoculations.

CUTANEOUS MANIFESTATIONS IN TRICHINOSIS. ANTON MUSGER, Dermat. Ztschr. **68**:34 (Nov.) 1933.

Musger reports a case in which extensive urticaria was the first symptom of trichinosis. Skin tests with muscle extract (Luger's test) were negative.

TAUSSIG, San Francisco.

DISTURBANCES OF THYROID FUNCTION IN SYPHILIS. EMIL PETRÁČEK, Česká dermat. **14**:105, 1933.

The author reports a unique case of diffuse miliary syphilitic infiltration of the skin with superimposed exfoliative dermatitis due to arsphenamine in a patient with classic symptoms of thyroid dysfunction. Biopsy confirmed the presence of syphilitic and nonsyphilitic changes in the skin. The patient showed an amazing response to thyroid therapy.

The basal metabolism was tested in eighty other cases of syphilis in various stages. In 75 per cent the rate was abnormal, in 70 per cent being above + 10

per cent. The effect of antisyphilitic treatment, particularly with neoarsphenamine, on the abnormal basal metabolism of syphilitic patients was studied in forty-two cases. The treatment brought the abnormal rate within physiologic limits (between +10 and −10 per cent) in the majority of cases.

Neoarsphenamine had no effect on the basal metabolism of nonsyphilitic patients (such as those with psoriasis or lupus erythematosus).

The toxicity of neoarsphenamine was studied in a series of animals in which hyperthyroidism or hypothyroidism had been induced. The result showed that in both states the body manifests decreased resistance to the drug. The author concludes his clinical and experimental observations with a statement that the glandulovegetative system, particularly the thyroid gland, plays an important part in the pathogenesis of syphilis and in the tolerance to antisyphilitic therapy.

Sudden Onset of Hemorrhagic Diathesis After Treatment with Sulphotreparsenan. Marie Runtova and George Černy, Česká dermat. **14**:267, 1933.

A woman, aged 40, had received four combined courses of antisyphilitic treatment. During the last three courses she was given bismuth preparations and Sulphotreparsenan (sulpharsphenamine) without any signs of intolerance. Half an hour after the fifth injection of Sulphotreparsenan in the fifth course, bleeding from the gums began. The hemorrhages assumed dangerous proportions. There were also epistaxis and subcutaneous hemorrhages, and the menstrual flow became profuse and prolonged. Under local styptic treatments and the application of tampons, a vitamin-rich diet and the administration of a blood coagulant, the bleeding was controlled in two weeks.

Spinka, Texarkana, Texas.

Glycogen and the Metabolism of Sugar in the Skin. Kenshow Narahara, Jap. J. Dermat. & Urol. **35**:229 (March) 1934.

In this study, in which the same general methods were employed as those described in previous communications, it was determined that the amount of sugar stored in the skin parallels that in the blood serum, even when the concentration of sugar in the blood serum has been caused to vary by means of various physiologic expedients (oral and intravenous administration of dextrose and injections of epinephrine, pilocarpine and insulin). The author concludes that the skin plays an important rôle as a temporary storehouse for sugar. With the same methods little change was noted in the amount of glycogen in the skin, and the conclusion is that the skin is of little importance as a receptacle for the intermediate products of sugar breakdown.

Sugar Storage in the Skin in Hunger. Eizaburoh Toshima, Jap. J. Dermat. & Urol. **35**:243 (March) 1934.

The author attempted to determine whether the amount of sugar stored in the skin suffers any diminution during periods of fasting. He found that even after a hunger period of seven days the sugar content of the blood and skin was within the normal physiologic limits for the nonfasting animal. The only change noted was a more abrupt rise and a shorter duration of the alimentary hyperglycemia in the fasting animal.

Sarcoid of Boeck. S. Harada and T. Hashimoto, Jap. J. Dermat. & Urol. **35**:276 (March) 1934.

A woman, aged 51, gives roentgenologic evidence of mildly active pulmonary tuberculosis. When she was 36 a hard infiltrated lump the size of the end of a finger appeared in the skin of the right hypogastrium. Since then other lesions of the same general character have appeared from time to time, until the temples, forehead, face, back, axillae, abdomen and loins at present show numerous diffuse,

largely confluent, occasionally slightly elevated areas of infiltration. Over these areas the epidermis shows reddish to dark brown pigmentation but otherwise is unchanged in appearance. Excellent photographs show that the lesions are most numerous and pronounced over the lower part of the back and the loins.

Photographs of microscopic slides exhibit both the histologic character of the lesions and later the effect of the roentgen treatments on them. Histologic examination proved the foci to be in the cutis, with an intervening cutical layer between the lesion and the almost normal epidermis, wherein traces of perivascular infiltration and thickening of the vascular endothelium here and there were all that seemed abnormal. The lesions themselves (before the roentgen treatments) consisted of isolated peripherally and centrally confluent, dense masses of lymphocytes, numerous plasma cells and a few epithelial cells. The intima of the vessels was thickened here and there. Giant cells and elastic fibers were absent.

Following irradiation there were visible only a few areas of moderate cellular infiltration and marked evidences of connective tissue development.

THE MEINICKE SECOND FLOCCULATION TEST (MEINICKE CLARIFICATION REACTION II). K. NISHIYAMA, Jap. J. Dermat. & Urol. **35**:289 (March) 1934

The Meinicke clarification reaction II was compared, in 3,637 serums, with the Wassermann and Murata reactions. It agreed with the Wassermann and Murata reactions in 88.69 per cent of cases, with the Wassermann reaction alone in 89.11 per cent and with the Murata reaction alone in 91.09 per cent. In occasional instances in which the serum was undoubtedly syphilitic and the Wassermann and Murata reactions were strongly positive, the Meinicke clarification reaction gave a negative reading; however, in these instances the reaction could be rendered positive by centrifugating the serum and controlling the reading under the microscope. The Meinicke clarification test II gave a somewhat higher percentage of positive readings in active serums, these extra readings being nonspecific. The nonspecific positives were somewhat less frequent with inactive serums.

Disregarding leprosy, the Meinicke clarification reaction II may be said to be specific for syphilis and to give fair results even with advanced conditions of hemolysis and putrefaction. The author concludes that it is an extremely simple and sharp-cut serum reaction and is to be highly recommended as a serodiagnostic aid.

SYPHILIS OF THE BLADDER. TOKUJI ICHIKAWA and RINZŌ SHINODA, Jap. J. Dermat. & Urol. **35**:301 (March) 1934.

In a 29 year old man the symptoms of florid secondary syphilis, including dysuria, were overcome by a few injections of arsphenamine. The dysuria, however, recurred later and disappeared only after 9 Gm. of neoarsphenamine and 21 Gm. of a bismuth preparation had been injected. Four instructive cystoscopic photographs clearly portray the papulo-ulcerous, slightly elevated lesions, grouped circularly about the air bubble at the apex of the bladder.

BRENNAN, Chicago.

LICHEN NITIDUS. B. RASZKES, Acta dermat.-venereol. **14**:375 (Dec.) 1933.

The author describes the clinical and histologic characteristics of lichen nitidus and discusses the points of similarity (especially in the early stages) and of differentiation between that condition and lichen planus. He describes two cases of lichen nitidus. In the first case the eruption on the hands and wrists showed clinically and histologically the typical picture of lichen nitidus, while the lesions on the legs bore all the characteristics of lichen planus. The lesions in the second case reminded one clinically of lichen nitidus, but the histologic changes were those of lichen planus. The author believes that a close relationship exists between these two dermatologic entities. He also mentions the possibility that a tuberculous

soil (first case) may play a part in building up the specific infiltration of lichen planus and thus transform it into lichen nitidus.

TUBERCULOUS ETIOLOGY OF ERYTHEMA NODOSUM. L. ROTNES, Acta dermat.-venereol. **14**:394 (Dec.) 1933.

According to the author, tuberculosis plays a prominent rôle in the etiology of the great majority of cases of erythema nodosum in children. However, the question of the tuberculous origin of this condition in adults is not settled. He reports the cases of four sisters, two adults and two children, living at home together, in whom typical erythema nodosum developed at the same time. All of them gave strongly positive Pirquet reactions. In the children roentgen examinations disclosed involvement of the lungs. In the two adults the roentgen examinations gave negative results. The husband of one of the sisters, who was tuberculous, had come to live with them shortly before they all fell ill; he apparently infected at the same time three other children in addition to the sisters. He died a few months later. The author believes that tuberculosis was the main factor in the etiology of these cases of erythema nodosum.

ETIOLOGY OF ALOPECIA AREATA. J. MERENLENDER, Acta. dermat.-venereol. **14**:404 (Dec.) 1933.

The author reports a case of alopecia areata which is especially interesting because in its etiology were found nearly all the factors mentioned in the literature as causes of this disease. According to the patient's history, physical shock and headaches preceded the appearance of the alopecia (trophoneurotic theory). Five men working in the same factory became affected with the same condition at the same time (epidemic character). Weakening of the patient's sexual power, pigmentary disorders manifesting themselves by a new growth of white hairs and followed by the appearance of vitiligo and, finally, lowering of the basal metabolism all point to an endocrine etiology. The author discusses the importance of histologic examination in forecasting the prognosis of alopecia areata. He found traces of pigment in the skin of the scalp and predicted a fresh growth of normal hair, which appeared a few years later. The author also discusses the growth of white hairs in the regions of alopecia areata and cites many authors who claim that this hair becomes normal in color sooner or later. He is of the opinion that there is some relationship between alopecia areata and vitiligo.

SEBORRHEIC ECZEMA AND THE PARAKERATOTIC DIATHESIS. H. REISS, Acta dermat.-venereol. **14**:424 (Dec.) 1933.

According to the writer, there is a group of skin diseases which includes seborrheic eczema, psoriasis, parapsoriasis, all kinds of parakeratotic erythrodermias and diffuse superficial purulent or mycotic dermo-epidermal eruptions. A common symptom of all these diseases is parakeratosis. They appear as a result of a special predisposition (diathesis) of the body, possible disturbance of the fat metabolism of the skin, parasitic influences, trauma, etc.

In most of the cases an intercellular exudate appears in the epidermis and is followed by an increase of the fat excretion, parakeratosis and scaling. The dysfunction of the glands of the skin (especially the sweat glands) as a sign of a general diathesis may also be an etiologic factor. The author enumerates the most important characteristics of this group.

TELANGIECTASIA HAEMORRHAGICA HEREDITARIA. F. FOLDVARI, Acta dermat.-venereol. **14**:427 (Dec.) 1933.

Telangiectasia haemorrhagica hereditaria is characterized by (1) heredity, (2) a tendency to the formation of telangiectasia and angiomas, mostly on the face, buccal mucosa, tongue and septum of the nose, and (3) hemorrhages which occur mostly

from the nose. It was first described by Osler in 1907, and 207 cases have been reported. The condition may be transmitted to both sexes and carried through many generations. The hemorrhages, which appear usually at the age of puberty, may be so frequent and severe that anemia or death results. The disease has nothing to do with hemophilia. The author reviews the literature on the subject. He reports a case of a family in which the patient, his father, an uncle, a brother, a sister and a daughter of the sister showed symptoms of telangiectasia haemorrhagica hereditaria. He also discusses the therapy of this condition.

VESICULAR AND BULLOUS LICHEN PLANUS. M. J. STRAUSS, Acta dermat.-venereol. **14**:447 (Dec.) 1933.

The author reports three cases of vesicular and bullous lichen planus with a description of the histologic changes in two. He gives a complete review and analysis of 78 cases found in the literature on this subject. The vesiculation in lichen planus occurs slightly more often in women than in men; age seems to be of no significance. The vesicle is usually subepidermal, rarely intra-epidermal. The author discusses the possibility of the vesicles and bullae being the direct result of arsenotherapy and concludes that this complication occurs without the use of arsenic. According to the author, the severity of the inflammation plays an important rôle in the appearance of vesiculation in lichen planus. He also believes that the occurrence of bullae or vesicles is probably dependent on an excessive amount of edema enlarging the preexisting microscopic spaces which are usually present.

TREATMENT OF PEMPHIGUS VULGARIS AND PEMPHIGUS CHRONICUS RECIDIVANS (MORBUS DUHRING) WITH BAYER 205. J. J. ZOON, Acta dermat.-venereol. **14**:473 (Dec.) 1933.

The author reports favorable results from the use of Bayer 205 in a case of pemphigus vulgaris and six cases of pemphigus chronicus recidivans (Duhring's disease). The medicine was well tolerated except for some after-effects, e. g., fever, albuminuria, toxic erythema, headaches and nausea. All of these complications were transitory. The author therefore recommends the use of Bayer 205 in the diseases mentioned. He insists, however, that this treatment should be given in a hospital under close observation.

SUPPLEMENTARY REPORT.—The patient with pemphigus vulgaris presented a recurrence of the lesions six months later; Bayer 205 was used without any success; the patient died a few months later. The same thing occurred in one of the cases of Duhring's disease. The author concludes that one should be reserved in the estimation of the permanence of the influence of Bayer 205.

PSEUDOREINFECTION IN SYPHILIS. N. A. TSCHERNOGOUBOFF, Acta dermat.-venereol. **14**:493 (Dec.) 1933.

The author describes a case of primary syphilitic ulcer on the prepuce with typical clinical and pathologic manifestations. Six and one-half months after the end of the treatment (two injections of 0.3 Gm. of arsphenamine and a few injections of mild mercurous chloride and mercuric salicylate) the patient came back to the hospital presenting a hard chancre on the abdomen, inguinal adenopathy, a typical secondary eruption, positive results of dark-field examination for Spirochaeta pallida and a positive Wassermann reaction of the blood. Because this chancre appeared more than four months after coitus and also because of the presence of well preserved remnants of the previous sclerosis on the prepuce, the author excludes the possibility of reinfection and superinfection and believes that this was a straight case of pseudoreinfection. He includes under this term cases of recidivation in which the process takes a course similar to that of a primary syphilitic infection, namely, chancre, adenitis, eruption and so on. These symptoms may be only faintly pronounced, or some of them may even be absent.

The author believes that many of the so-called reinfections are only pseudo-reinfections. The number increased with the beginning of the era of the use of arsphenamine. He is of the opinion that at the basis of the pseudoreinfection lies most probably Ehrlich's *sterilisatio fere absoluta,* or insufficient arsphenamine treatment, when all but a few spirochetes are rapidly destroyed but the process of development of the natural immunity of the body is disturbed, and as a result recidivation occurs. The author is of the opinion that the formation of the chancre (or of the pseudochancre) focus plays an important rôle not only in the initial course of the syphilitic process but in the subsequent ones (spirochetes' maturation focus?). Syphilis d'emblée and heredosyphilis seem to be the only exceptions to this rule. The author, however, found among ninety cases of syphilis d'emblée reported up to this time only five in which this diagnosis could not be challenged. They all presented a roseola, every lesion of which, according to the author, might be interpreted as some kind of a rudimentary hard chancre. He also considers the possibility of the syphilitic placenta being the initial lesion in heredosyphilis. The removal of the chancre results in the insufficient development of the immunity of the body. Recurrences not only on the skin, such as ulcus redux, but in the internal organs may be thought of as pseudoreinfections (*neurorécidives,* syphilis of the liver, etc.).

ASTRACHAN, New York.

Society Transactions

PITTSBURGH DERMATOLOGICAL SOCIETY

BERNHARD A. GOLDMANN, M.D., *Secretary*

Selected Cases from the Meetings of 1933-1934

FREDERICK AMSHEL, M.D., *President*

ONYCHAUXIS. Presented by DR. LESTER HOLLANDER and DR. J. W. FISHER.

L. G., American woman aged 23, presents an involvement of every nail of the hands and feet. The nail plates have lost their translucence; they are opaque, and there are areas where dark brown discoloration is present. All the lunulae are gone. The nails are raised convexly, causing the margins to have a curved appearance. This condition is of two years' duration. The patient has secondary syphilis of three months' duration.

Although onychosis and onychogryposis have been described by Sutton in syphilis, we do not believe that syphilis is responsible in this case and tend to the opinion that the condition of the nails is a manifestation of dyspituitarism.

DISCUSSION

DR. W. H. GUY: My associates and I have a similar case under our observation at the present time, and we found the patient to have a hypothyroid condition.

DR. LESTER HOLLANDER: This is the second case that I have observed in which a definite pituitary disturbance could be demonstrated.

HEREDITARY PROLONGATION OF LUNULAE OF NAILS. Presented by DR. LOUIS WILLARD.

This man, aged 25, states that his grandmother, father and one brother have had white nails since birth. Some of the patient's nails are markedly spatulate, and others are normal in contour. All are normal at the free edge and supra-ungual groove. All the nails are white, but in some, near the free edge, a narrow line of normal transparency can be seen.

DISCUSSION

DR. B. A. GOLDMANN: One might call the condition leukonychia rather than prolongation of the lunulae.

DR. LOUIS WILLARD: In answer to Dr. Goldmann, the nails are opaque, but there is some air or something else that produces the opacity of the nails in the little finger and the one next to it. There is a red line coming down close to the free edge of the nail which shows that the condition is only a prolongation of the lunula.

STOMATITIS AND DERMATITIS FACTITIA. Presented by DR. LESTER HOLLANDER and DR. C. L. SCHMITT.

A. L., a woman, aged 35, presents an indolent, necrotic, irregular tumefaction involving the greater portion of the right buccal mucosa. The condition is of one year's duration. In spite of various forms of examination, including biopsy, no reasonable diagnosis could be established.

She was first seen in September 1933. Under constant observation and treatment, although the mouth appeared better at times, there would be retrogression

of the lesion. On Feb. 6, 1934, the patient complained of an eruption which appeared suddenly on her arm. It was a typical artefact, quadrangular to rhomboid and abrasive. Since then other abrasive lesions have occurred which, the patient states, always occur after a chill and at night. This is the first case seen by us in which an artefact was produced on the buccal mucosa.

BRANCHIAL FISTULA. Presented by DR. STANLEY CRAWFORD.

W. S., a boy aged 5 years, had since birth a small opening, 1 mm. wide, immediately anterior to the crus of each ear about 1 mm. above the tragus. Each opening became slightly cystic at times, and a small amount of thick creamy material could be expressed. Frequent manipulation of the fistula in front of the left ear resulted in a large area of inflammation with pus, undermining the derma, and created a flat abscess 2 cm. in diameter. This abscess extends forward over the mandibular articulation. It is possible to insert a small probe into the fistulous opening for about 6 mm. Each area is a vestige of the first branchial groove. In embryonic life the ectoderm folds in to meet the outward-pouching entoderm in six distinct areas. The first branchial groove, or ectodermal infolding, forms portions of the ear and auditory canal, while the corresponding first entodermal outpouching, the first branchial pouch, forms part of the auditory canal and the tympanic cavity. In the case presented a vestigial first branchial groove formed a small fistula immediately in front of each auricle.

DISCUSSION

DR. EMERSON GILLESPIE: It is likely that the suppuration is caused by epithelial occlusion.

RELAPSE IN PRIMARY SYPHILIS. Presented by DR. J. C. KERR.

R. R., a white male aged 38, married and the father of six children, presents a large, typical chancre almost on the site of a previous lesion. There are indurated, painless glands which do not seem to be as hard as those usually found. The dark-field examination showed a large number of spirochetes.

The patient was first seen on Aug. 28, 1926, when he presented a lesion in the sulcus and on the corona. He applied for treatment on September 15, at which time the Wassermann reaction of his blood was 4 plus. He received eight intravenous injections of neoarsphenamine and ten intramuscular injections of mercury, which was followed by a thirty day rest. At the end of that time the Wassermann reaction was negative. He did not continue treatment, and on Jan. 27, 1927, just twenty-four days following the negative Wassermann test, he returned with a pea-sized lesion, sharply marginated, indurated and painless, on the opposite side of the penis. The dark field was teeming with spirochetes. Both he and his wife were referred to the McKeesport Hospital, where they received intensive treatment. After this he gave a negative Wassermann reaction on two occasions. No more treatment was given, nor was the regular Wassermann test check kept up. The patient was not seen again until he reported with the lesion now present.

DISCUSSION

DR. STANLEY CRAWFORD: It is difficult to say whether this chancre is a primary infection or a chancre redux, but I lean toward its being the latter, as it has occurred at the site of a previous chancre. This case may support the opinion of those who believe that there is an arsenic-resistant type of spirochete which has become more prevalent in the past few years.

DR. J. C. KERR: If the second lesion is a new infection because it is not on the site of the original lesion or in the lymphatic drainage area, the third lesion must also be a new infection, for the first lesion must have been completely cured. I believe that all the lesions are monorecidive or relapsing primary lesions.

FOLLICULITIS DECALVANS. Presented by DR. M. W. RUBENSTEIN.

S. G., a colored woman aged 27, presents an area of alopecia, the central portion of which consists of papules and pustules. The loss of hair has been progressive. The condition is of five years' duration. A similar condition began in the occipital region three years ago. She has employed various ointments without effect.

Microscopic study corroborated the diagnosis.

ERYTHEMA INDURATUM (STREPTOCOCCIC). Presented by DR. B. A. GOLDMANN.

Mrs. J. D., a white woman aged 29, presents several erythematous, tender, moderately edematous, subcutaneous nodules on the legs below the knees. There are also several depressed areas which show atrophy of the subcutaneous tissue and slight atrophy of the skin, which are the result of previous nodules.

The knees are distended with fluid but are not painful or tender, and there is an excess of synovial fluid in the tendon sheaths of the extensors opposite the left ankle joint.

This process has been recurring for the past ten years, and the appearance of the painful nodules has always been associated with the arthritis.

The patient had a periapical infection of her teeth and retained the lower left third molar mesial root. She also reacted to an intradermal injection of Streptococcus viridans (strain 2).

DISCUSSION

DR. S. A. NORRIS: I think that the condition is not erythema induratum but rather erythema nodosum, as the scarlike lesion on the left calf is not to be considered as entirely against the diagnosis of erythema nodosum. She has pain in the knees, a symptom associated with erythema nodosum, and the lesions are inflammatory and not ulcerated. There is desquamation of the lesion on the right anterior aspect of the leg.

DR. FREDERIC AMSHEL: I thought that the condition was erythema induratum, but after reading the history I think it may be erythema nodosum. The associated pain and all the other signs that accompany erythema nodosum would almost lead one away from the diagnosis of erythema induratum to make a diagnosis of erythema nodosum.

DR. W. H. GUY: I think that the condition is erythema induratum. The lesions are not particularly painful except on pressure, and the lesions have a fixed character, with no change from one month to another.

DR. EMERSON GILLESPIE: This woman has lesions which have disappeared and recurred. The condition began with involvement of the hypoderm, and later the epidermis was involved. I suggest the possibility of recurrent nonsuppurative panniculitis. Patients with this disease usually have some source of infection, as this patient has.

DR. W. H. GUY: Some of the pathologists today have a tendency to call panniculitis erythema induratum.

DR. H. T. PHILLIPS: I understand that the lesions have never broken down. I have never seen a case of erythema induratum in which they have not broken down. One sees cases of erythema nodosum in which they do break down, requiring complete curettement. I saw a patient who had three attacks in five years. During the last attack the lesions broke down, and it was necessary to curet them to heal them. Though such an outcome is unusual, such lesions do clear up in some instances. Since the lesions in this case do not break down, I should not call the condition erythema induratum.

DR. S. A. NORRIS: Have salicylates been used in this case?

DR. GEORGE BUSMAN: I think the question of diagnosis is a question of terminology. I believe that the condition is nondestructive erythema induratum without scarring. When I first saw the patient a year or two ago, she had

generalized lesions. The lesions are now bilateral, chronic and tender and occur on the posterior aspects of the lower parts of the legs. From the description I should call them erythema induratum, just as erythema nodosum can be tuberculous.

DR. B. A. GOLDMANN: Salicylates have not been given since the patient has been under my care. I think that the members are merely quibbling over terminology. The pathologic process began with a focus of infection somewhere in the body, which was streptococcic in origin. At various times the patient has had a bacteremia, with diffusion showers of organisms or toxins into the blood stream, which caused occlusion of the peripheral vessels, followed by infiltrative production of a cutaneous lesion and finally absorption, leaving atrophy of both the deep tissues and the skin. I agree with Dr. Busman that it is possible to have erythema induratum without any definite ulceration.

A CASE FOR DIAGNOSIS (ERYTHEMA INDURATUM?). Presented by DR. HOWARD T. PHILLIPS and DR. W. J. MORGINSON.

J. J., a white girl aged 10 years, presents chronic ulcers on the lateral and anterior surfaces of the legs. There are now three slightly indurated, rather superficial ulcers with undermined edges on the left leg and two similar ulcers on the right leg. There is only a moderate surrounding area of erythema and induration. These ulcers have been present for six months. There is a history of six similar, slowly healing ulcers which healed without appreciable scar formation. The case is presented as one of erythema induratum due to a toxin or a focal infection rather than to tuberculosis.

On June 18, 1928, the feces were normal in appearance; the benzidine test was negative; the fat content was slightly increased; Schmidt's test, showed no unchanged bilirubin; microscopic examination showed no pus, blood or ova; there was no undigested meat or starch.

On Dec. 30, 1933, the blood sugar was 99 mg. per hundred cubic centimeters.

On March 24, 1934, the Wassermann test of the blood was negative; the Kahn test was negative; the tuberculin test, with dilutions of 1:1,000 and 1:100, was negative. Urinalysis showed: an acid reaction; specific gravity, 1.025; no red blood cells; no albumin or sugar; from 3 to 5 pus cells per field, and no casts.

The ulcers were treated by thorough trimming of the edges and curetting of their bases; the application of boric acid compresses; the application of roentgen radiation, one-fourth skin unit, on Feb. 8 and March 2, 1934, and the administration of gold sodium thiosulphate, 10, 25 and 35 mg., on March 28, April 3 and April 10, respectively.

DISCUSSION

DR. F. M. JACOB: The girl is considerably overweight. She has definite cutis marmorata on both arms and legs. None of the active lesions show increased granulation tissue or induration, and I am inclined to think that the condition is not erythema induratum. I think it is an extreme cutaneous reaction to external irritation on a basis of glandular disturbance.

DR. LESTER HOLLANDER: I agree with the diagnosis of erythema induratum of Bazin. The patient shows Froelich's syndrome, and a definite endocrine disturbance. Patients with Froelich's dystrophia adiposa genitalis frequently show cutis marmorata. It is possible that on account of the endocrine condition the erythema induratum is not as characteristic as it might be.

DR. F. M. JACOB: Was the tuberculin test negative?

DR. EMERSON GILLESPIE: The tuberculin test was negative in dilutions down to 1:100.

DR. S. CRAWFORD: Could a histologic examination be made to rule out the possibility of tuberculosis, sarcoid or erythema induratum of Bazin?

DR. LESTER HOLLANDER: The negative tuberculin test is greatly in favor of erythema induratum. In cases of tuberculosis or erythema induratum of Bazin there is quite frequently an anergic reaction of the skin. I do not think that

clinically the condition is sarcoid, because sarcoid does not show the sinus formation and breaking down of the lesions that this child presents.

DR. H. T. PHILLIPS: When I first saw the patient she had only one lesion. I did not know what it was. I have had the patient under treatment for some time. There is sinus formation with overhanging edges. Under procaine hydrochloride anesthesia we curetted the lesion and cleaned it out and clipped off the edges—made it saucer-shaped instead of cup-shaped. Then later the other lesions came. The eruption was then fairly typical of erythema induratum. She gave a history of similar lesions in the past, which have healed. The laboratory work speaks for itself. The blood was normal; the tuberculin test was negative. We gave the patient 10 mg. of gold sodium thiosulphate. The pain disappeared, and the mother stated that the cutaneous condition was more than 50 per cent better. We gave her 25 and then 35 mg. of gold sodium thiosulphate, and shall continue with the latter dose. She has responded well. This drug acted as it does in lupus erythematosus. I am not certain that all cases of erythema induratum are tuberculous. They may be due to some other toxin. As the progress has been as good as it has, I hesitate to change the treatment.

MYCOSIS FUNGOIDES. Presented by DR. W. H. GUY and DR. FREDERICK AMSHEL.

This Italian woman, 44 years of age, presents an eruption of one and one-half years' duration. The condition began on the right leg below the knee as sharply marginated, slowly spreading, pruritic, annular lesions which gradually became infiltrated and underwent a superficial ulceration. Within the past three months new lesions have appeared on the arms, thighs and labia.

At the present time the right leg is involved from the thigh to the ankle. On the inner sides of the thighs and on the labia are dollar-sized infiltrated lesions. A section is presented.

DISCUSSION

DR. H. T. PHILLIPS: This case is certainly unusual. The lesions on the leg are not characteristic. Dr. Gillespie mentioned healing blastomycosis. I often wonder what happens to cases of so-called premycosis. This is one that apparently progressed to mycosis. If I remember rightly, Dr. Guy saw the patient several months ago and was not able to make a diagnosis of mycosis fungoides, or it was difficult to do so. At the present time I believe the diagnosis can be made.

DR. J. J. HECHT: Were any blood counts made? Has there been any change in the blood picture?

DR. M. W. RUBENSTEIN: What treatment has been given?

DR. W. H. GUY: In answer to Dr. Hecht, repeated blood counts were normal. There was no change in the blood picture. The case throughout has been interesting. When we saw the patient early, she had had the lesions on the leg for a year, and they were slightly scaly, erythematous, annular, slightly crusted, and intensely pruritic and had elevated and infiltrated borders. Laboratory studies were done by Dr. Robinson, who examined scales and found a pure culture of Alternaria. In tissue sections treated with special stains, we found that one section showed mycelia. Extracts were made and administered without any effect. The patient was given several injections. Repeated biopsy specimens were taken. The diagnosis was established by histologic examination. Two or three doses of roentgen radiation were given, and the lesions on the leg materially improved. The patient's general health does not seem to be affected to any great extent at the present time. The early sections, in contradistinction to the description of the premycotic state, were not diagnostic. The presence of cell nests in the epidermis was not noted. No granulomatous cells were seen, nor was there evidence of chorioma plaques. The last section from an infiltrated lesion led us to make a diagnosis from a histologic standpoint.

DR. M. W. RUBENSTEIN: I have seen patients respond to roentgen irradiation as given in Hodgkin's disease, that is, three-fourths skin dose to the lymphatic glands. I have no doubt that this condition will progress. I suggest malarial therapy. I saw one patient in particular who showed a marked response to that treatment and had no recurrence until two years afterward.

MELANOMA WITH CARCINOMATOUS NODULES. Presented by DR. LESTER HOLLANDER and DR. C. L. SCHMITT.

Mrs. A. K., a white American housewife aged 65, presents a progressive pigmentary disturbance of fifteen years' duration on the extensor surface of the forearm.

The condition began as a small, brownish-black discoloration and slowly evolved to its present size, 10 by 6 cm. Two nodular lesions having the characteristics of epidermoid carcinoma were found in the lesion.

DISCUSSION

DR. F. M. JACOB: This is one of the most interesting cases that have been presented. I suggest excision of the lesion for histologic study. It is known that melanoma progresses rapidly and may kill the patient in two or three months. Metastases sometimes occur in from two to twenty years. This condition is of fifteen years' duration and is evidently relatively benign.

DR. M. W. RUBENSTEIN: I differ with Dr. Jacob. I think the lesion should not be tampered with. Excision would be disastrous, even if it were wide. The patient does not show metastasis and should be given intensive irradiation.

DR. S. A. NORRIS: I think that it would be safe to excise the lesion, doubly safe with cautery dissection.

DR. J. C. KERR: Are the lesions on the face definitely metastases from the arm, or are they lupus erythematosus?

DR. H. T. PHILLIPS: I am not certain that the condition is melanoma. The patient may have a melanoma on the arm containing pigmentation, but the other lesions may be merely the same as those on the face. I am not certain that the condition will have a fatal termination in the next few years. Excision cannot be harmful. Removing material for study cannot make the condition worse if it is definitely a melanoma or sarcoma, and I am heartily in favor of securing material.

DR. F. M. JACOB: Ewing stated that melanoma is the result of excessive irritation of tissues. I believe that irritation of tissues is the cause of melanoma, by tars, smoking, chronic rubbing or what-not. The excess pigmentation causes irritation of the tissues and tumors may develop. Evidently it is not caused by malignant degeneration. This could be found out microscopically. It would do the patient no harm to lose some skin from the arm. I still think that excision would be of benefit to everybody concerned.

DR. LESTER HOLLANDER: I agree with Dr. Jacob, and I think that excision can be done safely with the electric knife. There would be very little danger from any operative procedure. Concerning the lesions on the face, one is definitely epidermoid carcinoma, unconnected with the lesions on the arm. The lesions on the arm are very unusual for this type of carcinoma. One of them seems to have pigmentation. We did not present the case as melanocarcinoma, because we believe it is a melanoma with carcinomatous degeneration. We shall continue with the case as suggested.

MELANOMA. Presented by DR. STANLEY CRAWFORD.

Mrs. A. G., aged 40, has a benign melanoma on the anterior surface of the left ear which measures 12 by 8 mm. The general shape is quadrangular, and the edges are straight and precipitate, the lesion being elevated about 2 mm. The

surface is mottled with dark brown and black pigment and does not show any infiltration of a neoplastic character. The lesion began as a pinhead-sized, dark brown spot twelve years ago and has gradually enlarged.

DISCUSSION

DR. EMERSON GILLESPIE: I consider this a case of seborrheic keratosis and should destroy it by electrocoagulation and irradiate it.

DR. F. M. JACOB: I disagree as to the treatment suggested, for I believe that the condition is due to degeneration of a melanoma or mole, and that it is a nevocarcinoma. Instead of destruction with cautery, I suggest excision followed by roentgen irradiation, and a study of the tumor.

DR. L. J. HECHT: The patient says that the lesion appeared twelve years ago. There was never any pigmentation before that. A nevus can appear later in life, of course, but it is significant that there was no involvement until twelve years ago.

DR. STANLEY CRAWFORD: There is a warty element in this case which is pigmented. If not pigmented at first, it became pigmented later. Keratosis does proceed with pigmentation. I do not know whether to leave the lesion alone. I am leaving it alone at present, and I advise excision and irradiation later.

PUSTULAR PSORIASIS. Presented by DR. LOUIS WILLARD.

R. C., an Italian woman, 36 years of age, first noted a few pustules on the ends of the thumbs ten years ago.

The skin at the ends of the fingers (except two) is now red, glazed and tense, and most of these bean-sized areas are sparingly dotted with minute pustules. The surrounding skin is hard, thick and dead-looking. The nails are deformed. She has a mold intertrigo of the upper, inner aspects of the thighs.

Ointment of ammoniated mercury and Whitfield's ointment both made things worse. One-half unit of roentgen rays caused temporary improvement. Suggestions as to treatment are requested.

DISCUSSION

DR. LESTER HOLLANDER: I consider this one of the most typical cases of acrodermatitis continué of Hallopeau that I have seen. It corresponds with the original description of that condition—a single finger, the thumb, being affected first after trauma, and then at long intervals finger after finger becoming involved. The cufflike protrusion of the skin and the color of it are characteristic. There was a good deal of discussion at the meeting of the American Medical Association in Milwaukee when Andrews and others read their papers on pustular eruptions of the palms. I somehow cannot consider that this condition is the same as that in Andrews' case. Other dermatologists have described cases as pompholyx, which is entirely different from this condition. I suggest treatment with ointment of mercuric nitrate, as in the famous case of Drs. Guy and Jacob, to see whether or not this ointment will be of benefit. I think it would be interesting to apply the ointment to one or two of the fingers to see whether it affects them.

DR. F. M. JACOB: I heard Dr. Andrews' paper also. He talked about pustular eruptions of the hands, the palms particularly, and the discussion then went on to pustular psoriasis and dermatitis repens. The patient that Dr. Hollander spoke about has since been presented in Cleveland as having pustular psoriasis with no question as to the diagnosis. He was completely cured after the members of the Pittsburgh Dermatological Society had tried everything without effect. Ointment of mercuric nitrate cured him temporarily, probably merely because it improves most eruptions. Since that time he has been presented at Cleveland with a diagnosis of pustular psoriasis.

DR. LESTER HOLLANDER: I do not agree that pustular psoriasis and acrodermatitis continué of Hallopeau are one and the same thing. At Copenhagen I

heard a very learned discussion, in which the consensus was that the two conditions are not the same.

DR. S. A. NORRIS: Has this case been going on for a long time? The nails are completely gone, and there is only a slight amount of soft material seemingly like nail structure. The general appearance of the ends of the nails is that of paronychia, but it ought to involve more of the nails.

BRONX DERMATOLOGICAL SOCIETY

HENRY SILVER, M.D., *Secretary*

Regular Meeting, Jan. 25, 1934

SAMUEL FELDMAN, M.D., *President*

A CASE FOR DIAGNOSIS (ERYTHEMA PERSTANS?). Presented by DR. LOUIS CHARGIN.

This woman, aged 23, single, a clerk, has been suffering from a disturbance of the skin of the face for two years. During this period the eruption has remained almost stationary.

The eruption is limited to the center of the face. It is superficial and slightly erythematous and occasionally shows a fine scaling. The outer limits of the eruption, located on the cheeks, are somewhat irregular. Adjacent to the affected area on the left cheek is a somewhat depigmented area the size of a dollar which resembles vitiligo. There are no subjective symptoms. For two years prior to the appearance of the lesions the patient had used once or twice monthly a bleaching wax which she applied not only to the face but to the neck. Yet there is no evidence of any involvement of the skin in the latter location. The process is not a pigmentation like that seen in argyria. It does not appear to be seborrhea, lupus erythematosus or dermatitis venenata.

Patch tests with a variety of cosmetics as well as with "mercolized wax" (the bleaching compound) proved negative. Chemical analysis of the wax failed to disclose the presence of either silver or mercury. The patient is in excellent health otherwise.

DISCUSSION

DR. A. ROSTENBERG: I assume that mercury is responsible for the process and that it has entered into combination with the tissues. I believe that the outlook for a cure is not good.

DR. A. SAYER: Deposits of mercury usually produce a slate color rather than the red that this patient's skin presents. Therefore, mercury is probably not responsible.

DR. D. L. SATENSTEIN: The erythema extends down to the neck. My impression is that it is due to atmospheric conditions and that it belongs to the chilblain group. Patients with such conditions have vasomotor instability and are influenced by both heat and cold, the condition attacking the exposed parts of the face and neck. I recommend the use of bland ointments.

DR. S. PECK: Though the eruption resembles greatly a seborrheic dermatitis, I believe that it represents a vasomotor disturbance, possibly produced or influenced by the cosmetics that the patient has used. I should try autohemotherapy, as I had good results in a similar case.

DR. I. M. LASHINSKY: It is posible that actinic rays produced a photosensitization, and hence the persistent erythema.

DR. L. CHARGIN: Possibly the patient is sensitive to light. A biopsy, to which she will not submit, might be of aid, especially from the standpoint of a chemical examination of the skin for heavy metals.

PITYRIASIS RUBRA PILARIS. Presented by DR. SAMUEL FELDMAN.

This woman, aged 65, about a year and a half ago noticed redness and scaling of the face and hands. The eruption spread a few months later to the feet, the trunk and the rest of the body. She was admitted to Mount Sinai Hospital about five months ago and was discharged two months later much improved.

The eruption is now fairly generalized. Mostly involved are the face, hands and feet. The eruption consists of numerous red, hard papules which are rough to the touch and possess tiny horny plugs. There is marked hyperkeratosis of the palms and soles. On the face and the backs of the hands the skin is red, thick, parchment-like and shiny.

The laboratory examination of the blood and urine revealed nothing abnormal.

KERATOMA PALMARE ET PLANTARE OR PITYRIASIS RUBRA PILARIS? Presented by DR. ARTHUR SAYER.

This white boy, aged 9 years, born in New York City of American parents, presented himself at the Morrisania Hospital dermatologic clinic on account of redness, scaliness and thickening of the palms and soles, said to have been present for a few years. The father denied that there was consanguinity of the parents. The patient's 6 year old sister and other members of the family have been examined and found to be entirely free from a similar eruption.

The patient presents symmetrical hyperkeratosis of palms and soles. The skin in these locations is reddish brown, thickened and slightly scaly. On the palms the condition extends from a little above the wrists to the tips of the fingers. The dorsal aspects of the terminal phalanges near the nails show a few hyperkeratotic plugs. The soles are uniformly thickened. There are no lesions on other parts of the body. The eruption has not caused any discomfort.

The laboratory tests of the blood and urine gave negative results.

DISCUSSION

DR. P. GROSS: Dr. Feldman's case is a typical one of pityriasis rubra pilaris, and Dr Sayer's case, that of the young boy, impresses me as an instance of localized pityriasis rubra pilaris.

DR. D. L. SATENSTEIN: The lesions shown by the boy impressed me as psoriasis, especially the palmar lesions. He shows no other evidence of pityriasis rubra pilaris. A biopsy would not aid much in the diagnosis.

DR. L. CHARGIN: In spite of the fact that the child does not show the typical picture of pityriasis rubra pilaris, I still consider that diagnosis. The condition is a special type of the disease and has been described in the literature. On the phalanges there is some follicular involvement.

DR. M. B. PAROUNAGIAN (by invitation): I cannot add much to what has been said. I should consider a diagnosis of keratoma palmare et plantare. Against the diagnosis of psoriasis is the absence of psoriatic lesions elsewhere.

DR. P. GROSS: Keratoma palmare et plantare would not be inflammatory, as this condition is.

DR. L. CHARGIN: Keratoma palmare et plantare would occur earlier in life and be found in other members of the family.

DR. H. KEIL (by invitation): There are some lesions on the boy's knees and elbows which have a distinct "nutmeg-grater-like" feel and would well fit into a diagnosis of pityriasis rubra pilaris.

Dr. A. Sayer: While it appeared to me that the clinical picture is that of keratoma palmare et plantare, I can see, in the light of the discussion, that the condition may be atypical pityriasis rubra pilaris. I shall investigate the case further.

Gumma of the Upper Lip. Presented by Dr. Samuel Feldman.

This man, aged 68, retired, states that eight years ago he had a "pimple" on the upper lip which was cauterized. It healed completely but recurred three years later. It has continued to increase in size.

There is now a large, hard, infiltrated ridge on the upper lip just below the nose. Part of the surface is verrucous. There are several copper-colored papules on the chin. The patient states that he has never experienced any pain and that itching has only occasionally been present. On the legs there are a number of scars from former ulcers which have persisted for many years.

The Wassermann and Kahn tests were negative.

Biopsy revealed distortion and elongation of the rete pegs. There was an increase in the number of blood vessels and fibroblasts. There was also a dense perivascular plasma cell infiltration.

DISCUSSION

Dr. S. Feldman: The biopsy demonstrated a plasmoma. Because of the more or less characteristic scars and in spite of the negative Wassermann and Kahn tests, I believe that the lesion of the lip is a gumma.

Dr. D. L. Satenstein: I cannot reconcile myself to a diagnosis of gumma. In two years such a lesion would either have broken down or have undergone fibrosis. The lesion is too soft. The histologic picture is not that of syphilis. I suggest a diagnosis of chronic lymphangitis.

Dr. F. Cross: I suggest a therapeutic test.

Dr. P. Gross: A definite tumor exists, and I suggest a biopsy, cutting deeply into the tissue when taking the specimen. It will not surprise me if the growth proves to be a basal cell epithelioma.

Dr. M. B. Parounagian (by invitation): Clinically the lesion does not impress me as a gumma. I should make a therapeutic test; if the test is negative, I should consider a diagnosis of rhinoscleroma.

Dr. D. L. Satenstein: Rhinoscleroma has a definite histologic picture and that reported by Dr. Feldman does not even remotely resemble it.

A Case for Diagnosis (Lymphangitis?). Presented by Dr. George J. Spinner.

This boy, aged 10 years, presents a linear lesion on the neck of six weeks' duration.

The involved area, about 3 inches (7.5 cm.) long, is situated on the left side of the neck and is wider at the upper pole. The entire area is red and infiltrated, and the surface is somewhat lichenified. There is no history of preceding chills or fever.

DISCUSSION

Dr. T. Rosenthal: There is a history that the lesion followed a haircut about six weeks ago. It is inflammatory and red, and there is a history of trauma. I should consider a diagnosis of lymphangitis.

Dr. E. F. Kelley: The linear form of the lesion as well as its short duration suggests a diagnosis of lymphangitis.

Dr. P. Gross: I do not know what type of lymphangitis this could be.

Dr. D. L. Satenstein: With the history of a preceding inflammatory reaction I should consider scleroderma en bande. Without considering this history, the lesion resembles a nevus.

DR. G. J. SPINNER: The lesion has progressed in the last week. That in itself speaks against a nevus. Permission for biopsy was refused.

LUPUS ERYTHEMATOSUS OF THE MUCOUS MEMBRANE OF THE MOUTH. Presented by DR. PAUL GROSS.

L. M., a white woman aged 26, single, American born, one year ago noticed a sore in the mouth. This condition cleared up but recurred about six months later. She consulted a dentist, who treated her for pyorrhea.

When seen on Nov. 28, 1933, she presented a patch about the size of a five cent piece, with a whitish center, showing definite atrophic scarring. The border was bright red and sharply outlined, with a number of telangiectases and a whitish, thickened epithelium covering part of the reddish area.

Roentgen examination of the chest showed increased hilar markings and thickening of the pleura at the apexes. Examination of the sputum gave negative results. No active foci were present in the lungs.

When seen again a few days ago the lesion in the mouth had increased in size, and there was another small patch on the lower gum. There was also a small lesion on the tip of the nose which had been present for about two weeks.

KAPOSI'S SARCOMA. Presented by DR. SAMUEL FELDMAN.

This woman, aged 34, states that following an injury to the left leg about two years ago she began to experience pain in the region of her left ankle. Three months later she noticed swelling and a "sore" which became very painful.

On examination there was a crusted, bluish-brown lesion over the left internal malleolus. Nearly the entire lesion was excised with the cutting current. The wound is healing, but the same dark blue color is visible in the newly formed scar.

Histologic examination showed evidence of new blood vessel formation. In many of the capillaries, the endothelium was thicker than usual, and occasionally there was more than one layer of cells. There were a number of enlarged lymph spaces, as well as dilated capillaries with a moderate amount of hemorrhage. Numerous pigment granules were found in the cutis. Most of the pigment was identified as hemosiderin with the iron stain. The cellular element in the cutis consisted of small numbers of well formed spindle cells.

DISCUSSION

DR. D. L. SATENSTEIN: If the central portion of the present lesion were removed, a true sarcoma would be found. This is not an uncommon complication of Kaposi's sarcoma.

DR. P. GROSS: How often has Dr. Satenstein seen true sarcoma develop from Kaposi's sarcoma?

DR. D. L. SATENSTEIN: I have seen three such cases.

MELANOCARCINOMA. Presented by DR. HENRY SILVER.

This American girl, aged 10, entered the Mount Sinai Hospital clinic on May 6, 1933, presenting a solitary, firm, somewhat bluish, elevated lesion the size of a hazelnut on the extensor surface of the upper part of the left thigh. The lesion had all the aspects of a benign nodule. The entire lesion was excised, and histologic examination revealed a melanocarcinoma.

The patient has been treated with radium, and at the present time, eight months later, there is a smooth scar at the site of the former lesion. There is no evidence of recurrence locally, and there are no palpable glands. The patient is in excellent health.

HENRY SILVER, M.D., *Secretary*

Regular Meeting, Feb. 23, 1934

SAMUEL FELDMAN, M.D., *President*

SARCOID (DARIER-ROUSSY'S TYPE)? Presented by DR. ADOLPH ROSTENBERG.

This colored woman, 50 years old, the mother of three healthy children, gives irrelevant past and family histories. The condition which she now presents began about one year ago with the appearance of a few nodules on the left arm.

On the upper part of the left arm and in the shoulder region there are six subcutaneous nodular lesions, varying in size from that of a cherry pit to that of a large almond; they are freely movable and irregular in outline, and some appear lobulated. Some of the lesions involve the skin, forming a solid tumor, on the surface of which are grouped deep red and violaceous papules the size of a millet seed. There are a few similar subcutaneous nodules on the back and on the right leg over the tibia. There is also a freely movable subcutaneous lesion in the left upper eyelid.

The Wassermann reaction of the blood was negative. A biopsy specimen was taken, but the result of the examination has not yet been reported.

DISCUSSION

DR. G. J. SPINNER: Not all the lesions are deep-seated; some are superficial. That speaks against the diagnosis of Darier-Roussy's sarcoid.

DR. D. L. SATENSTEIN: Darier-Roussy's sarcoid is not influenced by therapy; it usually remains deep and never extends up into the cutis but is always in the subcutis.

DR. C. GREENHOUSE: The single lesion on the leg is deep. May not this be a case of both superficial and deep sarcoid?

DR. D. BLOOM: I agree with the diagnosis as presented.

DR. A. ROSTENBERG: The lesion seemed to develop deep in the tissues and progress toward the surface. The lesion on the eyelid appeared simultaneously with the others.

LUPUS ERYTHEMATOSUS WITH LESIONS IN THE MOUTH. Presented by DR. LEO SPIEGEL.

This man, aged 22, a porter, was first treated for his skin condition in February 1930. He discontinued treatment after receiving a few injections of a gold compound. He reappeared in June 1932 and was then treated with twelve intramuscular injections of a bismuth preparation, after which he again discontinued treatment.

He returned again on Aug. 3, 1933, and up to the present time he has received thirty-six intravenous injections of a gold preparation. The condition has improved considerably.

He now has symmetrically placed, coin-sized lesions on the temples, cheeks and chin. They consist of flat, slightly roughened, purplish to brownish areas with central white atrophic and telangiectatic spots.

He is presented mainly to show the extensive involvement of the buccal mucous membrane. Here the lesions are bright red to purplish, with bluish-white areas of thickened epithelium where involution has taken place. The Wassermann test of the blood was negative. The slide precipitation test was also negative with both diagnostic and exclusion antigens.

DISCUSSION

DR. I. M. LASHINSKY: In my experience treatment with gold preparations does not influence lupus erythematosus in the mouth. Other measures of destroying the lesions are required. The high frequency spark might be of value.

DR. L. SPIEGEL: I believe that the response to bismuth was better than that to gold.

DR. D. BLOOM: I saw the patient five years ago. At that time he did not respond to bismuth therapy. At Bellevue the experience with bismuth has been disappointing.

DR. D. L. SATENSTEIN: I believe that curettage followed by cautery gives the best results.

DR. M. B. SULZBERGER: One does not see as many cases of lupus erythematosus with lesions in the mouth as one did formerly. Therapy seems to give good results at the onset but later fails. Even after destruction of the lesions new ones develop around the scars.

DR. D. L. SATENSTEIN: Many cases were formerly incorrectly diagnosed as lupus erythematosus of the mucous membranes, and that probably is the reason why one does not see so many of these cases.

DR. A. ROSTENBERG: Treatment with gold compounds was successful when first introduced but seems to be less so now. I cannot account for this. Carbon dioxide snow is still among the best remedies for this disease.

DR. S. FELDMAN: The therapeutic effect is most pronounced at the beginning, but after continued use the drug loses its effect.

DR. L. SPIEGEL: Dr. Rostenberg's contention with regard to the effectiveness of gold compounds is correct. The preparation used seems to be important.

GUMMA OF THE TONGUE WITH CARCINOMATOUS DEGENERATION? Presented by DR. LEO SPIEGEL.

C. R., aged 57, single, a watchman, who has been in this country for fifty years, states that he has had pain in the tongue for two months. He denies having had a venereal infection.

The tongue is somewhat enlarged and has a smooth, sclerotic, bluish surface. Extending through the long diameter of the tongue are two long, deep, irregular fissures with two pea-sized necrotic ulcerations. The tongue is hard on palpation and is painful near the necrotic areas.

The Wassermann reaction of the blood was 4 plus with two antigens. The slide precipitation test was 4 plus with both diagnostic and exclusion antigens.

DISCUSSION

DR. L. SPIEGEL: After an injection of a bismuth compound and one of neoarsphenamine the condition of the tongue improved greatly. I should like to know whether I am justified in taking a specimen for biopsy.

DR. A. SAYER: The consensus is that in syphilitic cases when there is a suspicion of carcinoma arsphenamine should not be given. A biopsy specimen should be removed with the electric cautery.

DR. D. L. SATENSTEIN: I observed a case several years ago in which carcinoma developed in a syphilitic patient under treatment, but nobody could prove that arsenic would produce proliferation of epithelial tissue. In all cases in which malignant growth is suspected one should get a specimen for biopsy as soon as possible, for the carcinoma is more important than the syphilis.

DR. G. ASTRACHAN: Sixty-five per cent of carcinomas of the mouth occur in patients with syphilis.

DR. M. B. SULZBERGER: Dr. Wise is of the opinion that arsenic will influence the growth of an epithelioma of the tongue or buccal mucosa, while Dr. Jadassohn

concurs with Dr. Satenstein. Arsphenamine does not contain the form of arsenic which causes cancer.

DR. S. FELDMAN: Dr Gottheil was against giving arsphenamine for a gumma of the mucous membranes. I think that arsphenamine improves such a lesion.

DR. L. SPIEGEL: Dr. Pollitzer is not opposed to giving three or four injections of arsphenamine in this type of case. I shall perform a biopsy and give bismuth meanwhile.

TERTIARY SYPHILIS? Presented by DR. SAMUEL FELDMAN.

This woman, aged 42, was admitted to the Morrisania Hospital on Feb. 16, 1934, suffering from chills and fever.

She states that about ten years ago she had an injury to her knee. Two years later she had an attack of chills and fever, accompanied by a rash and by bullae on the right thigh and buttock. She has had several similar attacks. The patient is married. She has one child, who is well. The husband is apparently well. She had had no miscarriages.

The left hip and buttock are red, swollen and tender. The margin of the red area is sharply outlined, and there are several bullae on the surface. The condition has been diagnosed as erysipelas. On the right hip and buttock there are numerous deep ulcerations, some of them punched out, and on deep pressure there is an exudation of pus so that some of these ulcers are thought to be blind fistulas.

Roentgen examination showed no involvement of bone. The reaction of the blood was negative to the Kahn test and strongly positive to the Wassermann test. Biopsy showed a perivascular infiltration of round cells and plasma cells and a certain amount of granulation tissue. There was no evidence of tuberculous structure.

DISCUSSION

DR. L. SPIEGEL: I should give the patient a therapeutic test.

DR. H. FEILER: My associates and I had a similar case in which the condition did not respond to any local treatment but cleared on antisyphilitic therapy. I believe that this patient has syphilis.

DR. E. F. KELLEY: I presented a similar case which was supposed to be one of actinomycosis, but one injection of arsphenamine cleared the eruption.

DR. D. L. SATENSTEIN: I think that the patient is malingering, and that the lesions are artefacts.

DR. R. BREAKSTONE: The lesions look like scrofuloderma.

DR. S. FELDMAN: Does erysipelas influence the Wassermann reaction?

DR. L. SPIEGEL: It may convert a negative Wassermann reaction to 1 or 2 plus but never to 4 plus.

DR. M. B. SULZBERGER: To my mind the therapeutic test is not convincing, because I have seen tuberculosis clear up with arsenicals. I also observed a case with a diagnosis of sporotrichosis in which when the exudate from the lesion was injected into a guinea-pig the animal died of tuberculosis, while the patient's lesions cleared up on treatment with iodides.

DR. S. FELDMAN: I shall bandage the affected side to prevent the production of artificial lesions, and as soon as the temperature comes down to normal I shall begin antisyphilitic treatment.

GLOSSITIS RHOMBICA MEDIANA. Presented by DR. LEO SPIEGEL.

B. S., aged 14, a schoolboy, was a patient in the nose and throat department of the Lenox Hill Hospital and was referred to the skin department because of the condition of his tongue.

On the dorsum of the tongue, anterior to the circumvallate papillae, there is a rectangular growth 2 by 2 cm. The lesion is sharply defined, lighter red than

the surrounding normal tissue, raised, smooth, shining and hard to the touch. There is no sensation in the affected area, and the patient was unaware of the condition until it was noticed by the physicians in the hospital. The Wassermann test of the blood was negative with two antigens, and the slide precipitation test was also negative with both diagnostic and exclusion antigens.

DISCUSSION

DR. L. SPIEGEL: The process is usually confused with syphilis. In the American literature I find two articles, one by Fordyce and Cannon (A Hitherto Unreported Condition of the Tongue, ARCH. DERMAT. & SYPH. **8**:749 [Dec.] 1923) and the other by Lane (Glossitis Rhombica Mediana, ARCH. DERMAT. & SYPH. **9**:547 [May] 1924). Fordyce and Cannon's two cases were both in persons with syphilis. The malady is supposed to occur only in adults.

Histologic examination shows sclerosis of the connective tissue. There is dilatation of the blood and lymph vessels, and cellular infiltration consisting of lymphocytes and plasma cells extends from the epithelium to the muscular tissue.

Brocq and Pautrier first described the condition, in 1914. They reported sixteen cases. Dubreuilh reported two cases. Arndt, in 1921, showed a case at a meeting of the Berlin Dermatological Society and reported that at his clinic a number of cases were seen in one year.

LUPUS VULGARIS. Presented by DR. GIRSCH D. ASTRACHAN.

This man, aged 49, white, born in the United States, states that he has always been in good health except for some bronchial trouble. The lesion began about twenty years ago on the right side of the neck. He was admitted to the Metropolitan Hospital on Feb. 29, 1932.

There is a palm-sized lesion 6 by 3 inches (15 by 7.5 cm.) over the right side of the neck, extending up to the mandibular process. The patch is sharply defined, and the edges are slightly elevated and nodular. The central portion shows areas of atrophy with fresh nodules in them. The nodules are salmon-colored and waxy in appearance. Apple jelly nodules are seen in some places under diascopic pressure. The patient is being treated with injections of old tuberculin twice weekly.

On examination, the urine was normal. Wassermann reaction of the blood was negative. A complete study of the blood chemistry revealed nothing abnormal. Roentgen examination of the chest gave negative results. The patient gave a positive reaction to old tuberculin in a dilution of 1:1,000,000 (intradermally). A biopsy showed typical lupus vulgaris.

DISCUSSION

DR. M. B. SULZBERGER: I have seen many patients with lupus vulgaris, and most of them required hospitalization. With reference to a salt-poor diet, Dr. Jadassohn is of the opinion that it has a beneficial effect; but the patients cannot stand it—they get salt hunger.

Among local measures, cross scarification is the best. The principle is to destroy the lupus nodules. As to drugs, common salt made into a paste and applied locally, though very painful, gives good results. The application of pyrogallic acid ointment in 10 per cent strength is also beneficial. Another method is irradiation with ultraviolet rays from a water-cooled quartz mercury vapor arc lamp every second or third day.

DR. D. BLOOM: At the Bellevue clinic my associates and I use electrocoagulation. As general treatment, the salt-free diet seems to be of value.

DR. A. SAYER: About three months ago I presented before this society a woman with lupus vulgaris of the face. In her case I am using curettage followed by local applications of boric acid ointment with a satisfactory result.

DR. L. SPIEGEL: I infiltrate the lesion with procaine hydrochloride and destroy it by electrodesiccation, then curet it out and apply a bland ointment.

DR. D. L. SATENSTEIN: For small lesions of lupus vulgaris I believe that surgical excision is the best method of therapy. One must be sure, however, to go through the fat down to the fascia, or the nodule may reappear in the scar. I do not like to use surgical diathermy in these cases because one cannot control the destruction of the surrounding tissue and the healing process takes longer.

A CASE FOR DIAGNOSIS (GRANULOMA ANNULARE?) Presented by DR. ISADORE M. LASHINSKY.

This young married woman, born in the United States, was seen in the Morrisania Hospital skin clinic on Feb. 7, 1934, presenting an eruption on the right hand and right foot, which had existed for about four years. The past history was uneventful. Physical examination gave negative results. The Wassermann test of the blood was negative. The urine was normal.

There is a circumscribed, somewhat infiltrated, round lesion, 5 by 5 cm., on the right hand. It is erythematous and slightly scaly and shows telangiectasia. It is situated on the dorsum of the hand and extends to the base of the index and middle fingers.

On the heel of the right foot there is a circumscribed, palm-sized lesion with a slightly elevated border, also scaly. In the middle of the lesion and as though attached to the achilles tendon there is a mass the size of a hazelnut, movable with the skin. On the medial side of the right toe, including the ball of the toe, there is an erythematous, scaly lesion. There is definite fissuring between the toes as well as scaling and mild itching.

The patient was treated in the Stuyvesant Square Hospital about one and a half years ago, where she received roentgen treatments of the hand and foot. Dr. Traub of that institution informed me that a tentative diagnosis of granuloma annulare was made, and that the patient received two erythema doses of x-rays at an interval of four weeks. Roentgen examination of the hand did not show cystic changes.

A biopsy made at the Stuyvesant Square Hospital confirmed the diagnosis of granuloma annulare.

DISCUSSION

DR. M. B. SULZBERGER: Clinically, the lesion on the hand especially is highly suggestive of granuloma annulare. The lesion on the foot resembles sarcoid. The etiology is of interest. Granuloma annulare is considered by some to be tuberculosis and by others to be sarcoid. The reaction to tuberculin is also of importance.

DR. D. L. SATENSTEIN: I do not consider the lesion on the foot granuloma annulare. It resembles sarcoid. The lesion on the hand, despite therapy, has increased in size.

Young women with a thin skin of the dorsum of the hand are prone to have dermatitis as a result of roentgen therapy.

DR. L. SPIEGEL: The lesion on the hand is granuloma annulare.

DR. A. ROSTENBERG: I do not think that the patient has radiodermatitis on the hand. The verrucous lesion on the foot complicates the diagnosis.

DR. S. FELDMAN: The only suggestion of radiodermatitis is the telangiectasia on the hand. Two erythema doses may have been more therapy than was intended One must consider a possible error of at least 25 per cent.

DR. D. L. SATENSTEIN: Erythema may sometimes follow even ¼ skin unit (70 roentgens). The error may be even 75 per cent. The dose tolerated depends largely on the susceptibility of the skin.

CHICAGO DERMATOLOGICAL SOCIETY

MAX S. WIEN, M.D., *Secretary*

Regular Meeting, Feb. 21, 1934

JAMES H. MITCHELL, M.D., *President, Presiding*

GLOSSITIS SYPHILITICA. Presented by DR. J. H. MITCHELL.

Mrs. B., aged 33, states that in August 1932 ulcerations developed on her tongue which were thought to be "canker sores." She was treated with metaphen, and the lesions cleared. They recurred, however, and later silver nitrate was applied. A biopsy was made, and the laboratory reported that the condition was a "sarcomatode." In November 1932 ten radon seeds were implanted. A severe reaction resulted and persisted for months. In December 1933 there developed marked swelling and ulceration somewhat similar to those which followed the radium treatment. This condition persisted until I saw the patient for the first time on Feb. 6, 1934.

The tongue was then much enlarged, lobulated and covered with thick membrane suggesting the eschar of a third degree radiodermatitis. Cultures incubated at room temperature yielded chiefly Staphylococcus aureus. Two Wassermann tests were negative. She had one child 11 years of age; later a miscarriage occurred at the third month.

The patient was given 0.3 Gm. of neoarsphenamine intravenously and gentian violet locally. On February 13 there was marked improvement. An injection of 0.45 Gm. of neoarsphenamine was then given, followed by a febrile and cutaneous reaction. She reported on February 21 greatly improved.

DISCUSSION

DR. C. W. FINNERUD: I failed to diagnose an epithelioma of Broder's grade IV, last spring, but I do not think that I shall miss one again. That variety can look much like sarcoma. I have heard that one of the members has entertained such a diagnosis for this patient's condition, but I cannot agree with him. I am of the impression that this is not a grade IV epithelioma but a granuloma. I cannot say definitely that it is syphilitic, but at least it is a granuloma.

DR. E. P. ZEISLER: Sarcoma of the tongue is one of the rarest conditions. Only two diagnoses can be entertained in this case, late gummatous syphilis and epithelioma developing in a syphilitic tongue. I think that as antisyphilitic therapy has brought about such striking improvement the condition possibly is syphilis alone, but one should keep the question of epithelioma in mind.

DR. RUBEN NOMLAND: I saw the sections before I saw the patient and thought that the condition was an epithelioma that had been treated with radium, but in view of the excellent results from neoarsphenamine I think that it probably is syphilis.

DR. DAVID LIEBERTHAL: I should like to have some light on the term "sarcomatode." This case teaches that in case of doubt one should use the therapeutic test, and from that point of view it is important. I shall not be surprised if the patient recovers under the treatment which Dr. Mitchell has instituted.

LENTIGO, GENERALIZED (SYSTEMATIZED NEVUS). Presented by DR. E. P. ZEISLER.

This woman, aged 28, states that she has had since birth innumerable brown and black freckle-like, pigmented spots on the arms, legs and body. Her face

is free. Her general health has been good. No other members of the family are similarly affected.

There is marked dermographia, which is not limited to the lesions. The facies is suggestive of a pituitary disturbance. There are literally thousands of freckle-like spots over the entire body, with the exception of the face; they are most numerous on the arms.

The blood count showed: erythrocytes, 4,460,000; leukocytes, 7,150; hemoglobin, 75 per cent. The systolic blood pressure was 90.

The results of biopsy will be reported later.

DISCUSSION

DR. S. W. BECKER: This is certainly a unique picture. The individual lesions correspond to those called lentigo because they are such a dark brown. The ordinary freckle is practically always yellowish brown. The patient's skin is not very dark. The lesions are not markedly worse on the exposed surfaces, and they are paler on the face than elsewhere, which eliminates xeroderma pigmentosum. She also has lesions on the palms, where I have never seen freckles but I have seen lentiginous lesions. I cannot offer any suggestions as to therapy or any explanation for the existence of the condition, and I agree with the diagnosis of generalized lentigo.

DR. FRED R. SCHMIDT: In an attempt to bridge the gap between urticaria pigmentosa and lentigo some dermatologists have described the type of lesion presented by this patient as xanthelasmoid nevus. Dr. Mitchell carefully isolated one of these lesions, and when it was rubbed definite dermographia took place in the lesion and not in the surrounding skin, which seems to substantiate the diagnosis of urticaria pigmentosa.

DR. F. E. SENEAR: I am inclined to agree with the diagnosis as presented. It seemed to me the patient had dermographia in all parts of the skin, and where the skin was stroked as a whole I saw no more reaction in the lesions than in the surrounding skin. Where the stroking was limited I thought that the edema in that part was due perhaps to the fact that only that area was rubbed.

DR. RUBEN NOMLAND: I am inclined to look on the condition as an abortive form of xeroderma pigmentosa. Dr. Montgomery reported several such cases a few years ago, some of which were not very different from this. I think that the final diagnosis will be revealed only by biopsy.

DR. J. H. MITCHELL: To my satisfaction I was able to palpate the urticareal lesions themselves in addition to the linear lesion of the dermographia. I am inclined to look on the condition as urticaria pigmentosa. I have had under observation for several years a patient with acquired urticaria pigmentosa who has as many lesions as this patient. A biopsy has been made in that case, and the diagnosis has thereby been confirmed.

DR. E. P. ZEISLER: I considered all the various conditions that have been mentioned today and arrived at a diagnosis by elimination. In my experience, the case is unique. I fail to see how one can make a diagnosis of xeroderma pigmentosum with the lack of involvement of the face. There are no keratoses and no leukodermic areas. The most striking lesions are on the trunk and extremities. In urticaria pigmentosa the lesions are much larger and fewer in number; here they are present by the thousands. The dermographia is not confined to the lesion but can be elicited everywhere. I shall try to get a biopsy specimen and work the case up further. In Germany dermatologists diagnose such lesions as generalized lentigo and classify them as systematized nevi.

SARCOID, LICHENOID. Presented by DR. F. E. SENEAR and DR. H. RATTNER.

This Negress, aged 28, who was born in Texas but has been in Chicago for eight years, presents a diffuse eruption of four years' duration.

The eruption consists of semisoft, brownish papules and nodules the size of a small pea on the neck, chest and upper part of the back and in groups on the arms. Most of the lesions are hemispheric; some are flat-topped and angular, with punctate depressions in the center. Some are shiny and on diascopic pressure are rather transparent. There are no subjective symptoms. The Kahn reaction of the blood was negative. The patient's general health has been unaffected except for asthma every winter during the past few years. General investigation by the medical department has not yet been completed.

Biopsy on a specimen taken from the elbow confirmed the diagnosis of sarcoid. In the upper part of the corium, extending to the flattened epidermis, were several tubercles which were closely aggregated. Each was composed almost entirely of epithelioid cells and had at the periphery a zone of lymphocytes. In the center of the larger tubercles there was early degeneration of the cells. The blood vessels were dilated and were surrounded by mantles of lymphocytic and epithelioid cell infiltration. No acid-fast bacilli were found.

DISCUSSION

DR. C. W. FINNERUD: I did not see the section, but if that bears out the clinical findings I agree with the diagnosis.

DR. E. P. ZEISLER: From inspection alone one would have to consider syringocystadenoma, but the histologic picture is so typical of sarcoid that there can be no question about the diagnosis.

DR. RUBEN NOMLAND: I have been studying several cases of sarcoid in Negroes with lesions varying from the size of those that this patient presents to large nodules. To my mind, this woman presents typical papular sarcoid with lesions chiefly on the trunk, while in the cases of papular sarcoid that I have observed the lesions were located exclusively on the face and neck.

DR. F. E. SENEAR: We had exactly the same feeling that Dr. Zeisler expressed when we first saw the small shiny lesions on the chest. We thought of syringocystadenoma as a strong possibility but considered sarcoid as an alternative, and the biopsy settled the diagnosis.

PRURIGO NODULARIS. Presented by DR. J. H. MITCHELL and DR. R. H. SCULL.

This white man, aged 65, presents an eruption of thirty years' duration, accompanied by pruritus. He states that it began as a pruritic dermatitis on the head, shoulders, arms and hands. The condition has persisted but has remained practically limited to the head most of the time. The skin of the neck and ears, and to a lesser extent that of the face, has gradually become thickened and now presents a profuse eruption made up of pea-sized and larger semiconfluent, intensely pruritic nodules which are the color of the normal skin. There was a single hazelnut-sized pruritic nodule on the left arm.

This large nodule and one from the neck were removed for study. Both showed essentially the same changes, moderate hyperkeratosis and parakeratosis and marked, irregular acanthosis. Around the blood vessels and the deeper cutis were thick mantles of cells, made up chiefly of lymphocytes but also containing a few mast and plasma cells. There seemed to be hypertrophy and sclerosis of the collagenous tissue.

DISCUSSION

DR. S. W. BECKER: My associates and I have a patient in the hospital who has typical prurigo nodularis; some of the lesions have been present for thirty years. She is an extremely unstable person with neurocirculatory disturbance. She occasionally presents lesions that are typical of neurodermatitis but still retains these nodules. It is interesting that the pruritus occurs as the barometer goes down. She can predict changes in the weather as well as a person with long-standing tabes. I have not had enough experience with prurigo

nodularis to hazard an opinion, but Dr. Pautrier told me that prurigo nodularis, lichen obtusus corneus and multiple circumscribed nodular lichenifications are one and the same condition.

DR. MAX S. WIEN: The exaggerated picture of the neurodermatitis suggests a diagnosis of neurodermatitis gigantea, cases of which were reported by Merenlender (*Arch. f. Dermat. u. Syph.* **161**:6 [June] 1930). In those cases there was also a tendency to nodule formation and verrucous-like proliferation in the patch.

DR. R. H. SCULL: When we first saw this man, our impression was that the condition might be classed as atypical prurigo nodularis. This impression is further substantiated by the history and the histologic structure of lesions removed from the neck and the upper part of the left arm. The histopathologic picture of the two lesions was not unlike that in a typical case of prurigo nodularis shown before the society last year.

PURPURA ANNULARIS TELANGIECTODES. Presented by DR. F. E. SENEAR and DR. HENRY SCHORR.

Mrs. J. M., aged 46, foreign born, presents a patchy dermatosis of two months' duration. The lesions are irregular, rust-colored and somewhat reticulated. Tiny punctiform insets of purpura may be noted. The lesions vary slightly in the state of evolution, the older ones tending to become whitish and to show delicate atrophy. She also presents diffuse, poorly defined patches of dermatitis on the extensor surfaces of the upper extremities; the lesions show a definite wheal-like character and moderate pruritus.

Biopsy on a specimen taken from the leg showed histologic changes characteristic of purpura annularis telangiectodes. The epidermis showed a thin parakeratotic scale and moderate intracellular and intercellular edema. Throughout the corium, including the papillae, were endarteritis, hyalinization, thrombosis and organization of most of the blood vessels, only a few remaining open. About the vessels and sweat glands were noted dense mantles of infiltration composed of histiocytes, lymphocytes and fewer polymorphonuclear leukocytes, and about the vessels lay many extravasated red blood corpuscles. The thrombosed vessels contained many fat droplets, demonstrated by the sudan III stain. The ferrocyanide stain showed blue granules of hemosiderin about the vessels, and the van Gieson and Weigert stains showed loss of collagen and elastic fibers in all zones of infiltration.

DISCUSSION

DR. E. P. ZEISLER: I dislike to dissent with the diagnosis that was presented by those who have given more careful study to the case than one is able to do here, but the picture does not agree with my conception of Majocchi's disease. I did not see the typical cayenne pepper puncta or any annular lesions. There are some varicosities on the lower extremities which could easily account for the pigmentation. There are some lesions on the upper extremities which I could not identify. I hesitate to record the case in the literature as one of Majocchi's disease, which is a rare condition.

DR. RUBEN NOMLAND: I agree with Dr. Zeisler.

DR. J. H. MITCHELL: I observed this patient with a great deal of interest. The annular lesions typical of Majocchi's disease are absent, but there is atrophy, and it seems to me that there are enough telangiectasia and purpura to establish the diagnosis. One always looks for these cases and seldom finds them.

DR. M. H. EBERT: Were changes in the blood vessel walls present?

DR. F. E. SENEAR: We did not intend to present this patient with a diagnosis of purpura annularis telangiectodes. When we first saw her she presented lesions on the upper and lower extremities, and at that time the lesions on the upper extremities were very different in type, simply an erythematous dermatitis, a toxic process. At that time there was distinct purpura in several of the lesions on the

legs. We considered Schamberg's disease and simple hypostatic dermatitis and merely mentioned the possibility of Majocchi's disease. Biopsy was done and it was reported that the histologic picture was typical in every respect of that described for this disorder. I have seen the slide only as shown on the screen, but there Dr. Caro pointed out the vascular changes as well as the others described by Majocchi. We hesitated to put the case on record on the basis simply of the histopathologic observations because the condition is so rare. I recall only two cases shown before this society, one by Dr. Mitchell, in which I think the diagnosis was disputed. I do not remember who showed the other case. We do not insist on that diagnosis but feel that it is a possibility.

A Case for Diagnosis (Pityriasis Lichenoides Acuta?). Presented by Dr. S. W. Becker.

This man, aged 54, presents an eruption which appeared on the arms and legs about two months ago. It spread to involve the entire body, with the exception of a region above the neck and the palms and soles. The lesions had been appearing up to the time of his admission to the hospital, three weeks ago. There have been no appreciable subjective symptoms.

Physical examination gave negative results. The Kolmer and Kahn reactions of the blood serum were negative, and the urine was normal.

Over the entire body, with the exception of a region above the neck and the palms and soles, are discrete, nonindurated papules, chiefly from 0.5 to 0.75 cm. in diameter, with slight scaling. The color varies from yellowish red to dark red, and the lesions on the legs were purpuric. The patient also has tinea versicolor.

Histologic examination showed the stratum corneum to be slightly thickened and loose. The stratum granulosum was absent intermittently, and in these regions there were small intra-epidermal pustules. The epidermis was slightly thickened and showed intercellular edema and considerable cellular infiltrate. The papillae and superficial dermis were edematous and involved in a perivascular round cell infiltrate which extended deeply along the blood vessels and was found about sweat glands.

DISCUSSION

Dr. F. E. Senear: It is, of course, impossible to get the impression today that would have been gained had the patient been seen earlier, but the good photographs shown, I think, enable one to visualize the condition fairly well, and the combined evidence of the photographs and the remaining lesions almost perfectly establishes the diagnosis of pityriasis lichenoides varioliformis et acuta.

Vulvitis (Ulcerative) and Stomatitis. Presented by Dr. M. H. Ebert and Dr. M. J. Wolff.

Mrs. M. F., aged 38, married, states that during the past six years she has had recurrent ulcers on the tongue and occasionally on the buccal mucosa. At first these lesions appeared about every six months and lasted two weeks, but during the past two or three years they have recurred more frequently and lasted longer, and during the past year a lesion has been present almost constantly.

During the past eighteen months, in addition to the lesions in the mouth there have appeared lesions at the outlet of the vagina. The first one remained about five weeks and healed. Later similar lesions appeared at shorter intervals and persisted longer, so that now a lesion is present almost constantly. These lesions have been so painful at times that the patient was unable to walk.

Her family history was irrelevant, with no history of mental disorder. She has been married for twenty-one years and has had ten pregnancies, seven of which ended in self-induced abortions. Three children are living and well. Her husband is living and well. Menstruation began at 15; the periods last five days and occur regularly every twenty-eight days. Two years ago she underwent

bilateral salpingectomy and cauterization of the cervix. She states that she has been nervous for from twelve to fourteen years and that this condition is gradually becoming worse.

There is now an irregular ulcer about 2 by 4 cm. in diameter and from 2 to 3 mm. deep on the inner surface of the left labium minus. The walls are slightly sloping; the base is not infiltrated and is covered by a yellowish exudate. There is no inflammatory areola about the ulcer. On the inner surface of the right labium minus is a similar but smaller ulcer. There is considerable purulent vaginal discharge, but no lesions are present on the cervix.

On the left side of the tongue there is a shallow ulcer about 2 mm. in diameter, covered with a slight exudate, now in the process of healing.

The laboratory findings were essentially negative. The blood count showed: hemoglobin, 70 per cent; erythrocytes, 5,110,000; leukocytes, 7,850; polymorphonuclear neutrophils, 63 per cent; lymphocytes, 22 per cent; mononuclears, 6 per cent; eosinophils, 7 per cent, and basophils, 2 per cent. The Wassermann reaction of the blood and of the urine was negative. The basal metabolic rate was —20 per cent. Smears made from the ulcers were negative for Bacillus crassus. Roentgenographic examination of the chest revealed nothing abnormal.

DISCUSSION

DR. C. W. FINNERUD: I do not know with what diagnosis the patient was presented, but I believe that conditions such as this, with associated lesions in the mouth and vulvar region, are undoubtedly something apart from the disease described by Lipschütz as "ulcus vulvae acutum." In most of these combined cases, B. crassus has not been found in the vulvar lesions, and when lesions are present in both areas I think that they are commonly even more painful than those of true ulcus vulvae acutum. Whether conditions such as this belong with periadenitis mucosa necrotica or with the aphthae I do not know.

DR. MAX S. WIEN: The vulvar lesions resemble some of those in the group described by Neumann, who in 1895 reported thirteen cases of aphthous ulcers of the genitals, eleven of which were associated with lesions in the mouth such as those presented by this patient. The question has been raised as to the relation of this case to that reported by Dr. Perlstein and myself (*J. A. M. A.* **98**:641 [Feb. 6] 1932). The lesions in Dr. Ebert's case are much deeper and more chronic that those in our case, and B. crassus was obtained in pure culture from the vulvar lesions in our case. If a condition is to be properly classified as ulcus vulvae acutum (Lipschütz), B. crassus must be present in the lesions. Although this disease usually has a short course it may follow a chronic course with recurrences. One of Lipschütz' patients was under his observation from 1909 to 1918 and had six relapses. There has been considerable discussion as to the relation of the oral and vulvar lesions in cases of ulcus vulvae acutum (Lipschütz) associated with lesions of the mouth because of the absence of B. crassus in the oral lesions. Matras (*Arch. f. Dermat. u. Syph.* **166**:491, 1932) reported a case in a girl, aged 13, who presented the clinical picture of aphthous erosions and ulcerations on the oral mucous membrane and genitalia (ulcus vulvae acutum); B. crassus was found in the genital and oral lesions microscopically and culturally and also in the blood culture. Matras felt that the finding of B. crassus in his case was proof of the etiologic relationship of the genital and oral manifestations.

DR. J. H. MITCHELL: Were any other findings made in the smears, positive or negative for B. crassus?

DR. M. H. EBERT: I think that such ulcers of the mouth and vulva are extremely hard to classify since there is no cleancut criterion of etiology. The closest approach to it is in the group described by Lipschütz as ulcus vulvae acutum, in which B. crassus is present in almost pure culture in the vast majority of cases in the lesions of the vulva and has recently been reported in the oral lesions. There is a question whether B. crassus is the sole etiologic agent. Auto-inoculation experiments have given uniformly negative results. However, this group comes

near to being a cleancut entity. There is also the group described by Neumann in which there are aphthous lesions on the genitalia and in the mouth, associated in many instances with evidences of multiform erythema with rheumatic changes in the joints and in some instances with erythema nodosum; this would lead one to believe that some of these cases are infectious, but this cannot be proved. There is a third group in which an angiospasm may cause the lesion. The clinical findings have varied greatly. Lipschütz described all types of lesions, from those the size of a pinhead on the genitalia to the large necrotic ulcers that start with fever, chill and malaise and result in necrosis. I think that the case presented today fits in best with the aphthous group of Neumann.

MORPHEA AND SCLERODERMA OF THE HANDS. Presented by DR. E. A. OLIVER.

This white woman, aged 30, was first seen on Feb. 19, 1934, complaining of lesions on the back which had been present for eighteen months, lesions on the abdomen which had been present for one year and involvement of the hands and fingers for the past eighteen months. She states that she feels well except that the hands become blue and painful when they are exposed to cold.

Her basal metabolic rate was —8 per cent.

The patient presents in the right subscapular region and on the right side of the abdomen a number of irregular-shaped, dime-sized, ivory-white areas with scalloped outlines. The entire group is surrounded by a violaceous border.

In some of these ivory-white areas are depressed points resembling the patulous orifices of sebaceous glands.

The fingers of both hands are stiff, and the skin of the fingers seems bound down to the underlying tissues.

DISCUSSION

DR. E. P. ZEISLER: I offer the diagnosis of Hallopeau's disease. In the cases that I have seen scleroderma of localized type has been smooth and ivory-like. These lesions have an atrophic-like scale and some contain plugs, and I think that the diagnosis of Hallopeau's disease should be considered. I was unable to demonstrate to my satisfaction any sclerodermatous changes in the hands.

DR. RUBEN NOMLAND: I think that the lesions on the back present typical cardlike scleroderma. The most typical lesion that I could find was a macule not over 2 mm. in diameter, flat, white and not elevated. That is probably the distinguishing feature of cardlike scleroderma in differentiation from Hallopeau's disease, in which the elementary lesion is a white papule. The question of plugging is not of as much importance in the diagnosis as the textbooks lead one to believe, for I have seen plugging not only in scleroderma and in Hallopeau's disease but in simple lichen planus, which has left atrophy. I think that the condition is an interesting combination of superficial cardlike scleroderma and early sclerodactylia.

DR. C. W. FINNERUD: I doubt whether in the absence of the changes which are present on the hands and feet many dermatologists would be sure that the condition was morphea. Because of the few comedo-like keratotic plugs that are present in all the lesions, I should be inclined, in the absence of the lesions of the hands, to make a diagnosis of Hallopeau's disease.

DR. F. E. SENEAR: I saw the patient with Dr. Oliver, and we both considered the diagnosis of Hallopeau's disease as an alternative diagnosis, but in view of the violaceous border and the elementary type of lesion which Dr. Nomland described, I agreed with Dr. Oliver that the condition was morphea or circumscribed scleroderma.

DR. E. A. OLIVER: I examined the patient carefully this morning with Dr. Senear. While one sees stippling in the ivory-colored patches there is no real plugging such as is seen in lichen planus sclerosus et atrophicus. The lilac-colored borders together with the beginning sclerodactylia make me certain that the condition is circumscribed scleroderma.

JAMES H. MITCHELL, M.D., *President, Presiding*

Regular Meeting, March 21, 1934

MAX S. WIEN, M.D., *Secretary*

PARAPSORIASIS? Presented by DR. RUBEN NOMLAND and DR. M. J. WOLFF.

This man, aged 64, first noted an eruption about four years ago. He states that it began as "red spots" on the legs, gradually extending to the thighs, abdomen and chest. There has been some tendency to variation in the intensity of the eruption, but it has been present since the onset, accompanied by moderate pruritus.

His general health has remained good, and physical examination revealed only a moderate infection of the prostate, an inguinal hernia and bilateral varicose veins. The Wassermann reaction was negative.

The eruption is present over the entire body except the palms and soles. It is not pronounced on the legs and arms and less marked on the trunk, and there is a minimal amount on the face and scalp. Superficial examination suggests only a generalized erythroderma with some scaling and questionable (senile?) atrophy. On closer examination it may be seen that the eruption in some areas consists of scaling papules of various sizes.

DISCUSSION

DR. H. M. HEDGE: The generalized distribution of this ichthyosiform eruption and the amount of pruritus make me think of aggravated ichthyosis. The scales are very thin, and while the condition is of four years' duration the pruritus is a little too severe for parapsoriasis. Moreover, the fact that the condition extends to the face and scalp suggests ichthyosis rather than a toxic condition.

DR. H. R. FOERSTER: I consider this a typical case of pityriasis lichenoides chronica. The mild subjective symptoms do not oppose that diagnosis.

DR. L. F. WEBER: I think that the eruption is generalized parapsoriasis. I believe that as a rule one does not see ichthyosis with an inflammatory phenomenon.

DR. A. W. STILLIANS: The patient may have ichthyosis with parapsoriasis.

DR. MAX S. WIEN: The discreteness of the lesions and the general character of the eruption suggest the diagnosis of pityriasis lichenoides chronica. The patient said that there is some pruritus, but I was impressed by its mild character after questioning him.

DR. J. H. MITCHELL: I saw the patient in the clinic yesterday and discussed at length the connection between the condition and a possible lymphoblastoma. While I was talking with him and watching him there seemed to be rather mild pruritus. I shall try to get a specimen for biopsy in order to determine the diagnosis.

SYRINGOMA. Presented by DR. RUBEN NOMLAND, DR. D. V. OMENS and DR. R. H. SCULL.

This Negress, aged 26, states that an eruption appeared on her face when she was about 8 years old and that the lesions have slowly increased in number since then.

The eruption now consists of oval papules 1 mm. in diameter, the color of the surrounding skin, situated about the eyes and on the cheeks, forehead and chin. No subjective symptoms are present.

A biopsy specimen was taken, but because of an accident in technic, no satisfactory sections were obtained. Study of the sections available showed definite small cystic areas made up of two rows of cells and containing amorphous material. Definite strings and cords of cells were not seen, although there was a suggestion of such structures.

DISCUSSION

DR. M. H. EBERT: I saw this patient and thought that the condition might be the result of a sebaceous change. In the cases of syringocystoma that I have seen the tumors have been more hemispheric, larger and not so numerous.

DR. M. R. CARO: Histologically I think that the condition is syringocystoma.

DR. MAX S. WIEN: My clinical impression was that of syringocystoma.

DR. RUBEN NOMLAND: The classification of such nevoid lesions presumably arising from the sweat glands is difficult. Reading the two or three standard textbooks on histopathology seems to lead more to confusion than to anything else. However, I believe that a diagnosis can usually be made clinically in these cases and that it can be proved by histologic examination. The lesions are papules, practically the color of the skin, somewhat flattened and most frequently found on the eyelids. We have observed two cases in which we made the diagnosis clinically and proved it histologically, and I think that in most of the cases the condition falls into the classification given by Gans as "syringoma." As far as I can judge the term "syringocystadenoma" refers to a slightly different entity but one which also has its origin from the sweat glands.

A CASE FOR DIAGNOSIS (TUBERCULOSIS VERRUCOSA CUTIS?). Presented by DR. HERBERT RATTNER and DR. M. R. CARO.

A boy, aged 12, born in Chicago, presents a lichenified patch of several years' duration on the right buttock. He does not recall how it started, but apparently it has not enlarged.

The lesion is sharply defined and elevated from the surrounding skin. It is the size of a silver dollar, purplish and lichenified, has an irregular top and is covered by a scant, adherent, dry scale. The center of the lesion has involuted. There is no pruritus.

The results of general physical and laboratory examination were normal.

On histologic examination the epidermis showed acanthosis with irregular lengthening of the rete pegs and a thin, non-nucleated scale. There were moderate intracellular and intercellular edema, a discontinuous granular layer and a basal layer which in many places was disorganized by the invasion of infiltrating cells from below. In the papillae the blood vessels were dilated. Here and in the subpapillary layer was noted a dense infiltration of lymphocytes, histiocytes, plasma cells and a few polymorphonuclear leukocytes. Mantles of similar infiltration extended along the blood vessels and sweat glands.

DISCUSSION

DR. H. M. HEDGE: This lesion appeared to me on first inspection as a tuberculid, but the histologic examination did not reveal any tuberculous structure. It showed a chronic inflammatory reaction or the structure of a verruca or nevus. The color and the definite circumscribed borders of the nodular lesions made me think of tuberculid, but I have to withdraw that impression in consideration of the histologic evidence.

DR. E. A. OLIVER: The condition impressed me as tuberculosis verrucosa cutis. I examined the histologic section carefully and believe that the picture is not incompatible with that diagnosis. There was marked cellular infiltration extending between the papillae, and I detected one giant cell in this infiltration. Clinically the eruption is tuberculosis verrucosa cutis.

DR. A. W. STILLIANS: I agree with Dr. Oliver.

DR. M. R. CARO: Dr. Rattner and I thought that clinically the condition resembled tuberculosis verrucosa cutis, but we thought that we could rule out that diagnosis on histologic grounds. The epithelioid cells were comparatively few, and the predominant cells were lymphocytes. The one giant cell I thought was a foreign body cell. We shall try to inoculate a guinea-pig and report the results later.

DR. RUBEN NOMLAND: We have observed two cases of tuberculosis verrucosa cutis in which practically no tubercles were found on biopsy, but in one case the results of guinea-pig inoculation were positive. In other words, in tuberculosis verrucosa cutis there may not be a very marked tuberculous reaction.

DR. J. H. MITCHELL: This case reminded me of one that Dr. Nomland and I demonstrated two years ago, in which there were large lesions on the flexor surface of the wrist. I believe that the condition is tuberculosis verrucosa cutis.

NOTE.—Inoculation of a guinea-pig gave negative results.

IODIDE ERUPTION, ERYTHEMA NODOSUM TYPE. Presented by DR. MAX S. WIEN and DR. MINNIE O. PERLSTEIN.

This white woman, aged 48, with tabes dorsalis, received treatment with mercurial inunctions and saturated solution of potassium iodide by mouth.

She was first seen on Feb. 14, 1934, when she presented numerous painful, discrete, coin-sized, erythematous nodules over the anterior aspects of both legs, with a lesion the size of a half-dollar on the left calf. She stated that these lesions were of one month's duration and that they seemed to come and go. The lesion on the left calf presented a slight amount of central softening, but the skin over this lesion was intact.

She had been receiving iodides for about three weeks before the lesions appeared. The administration of iodides was stopped, and the patient was seen again on February 28, with complete clearing of the condition. The treatment with iodides was then resumed, and at the present time there is a single, coin-sized, nodose lesion over the right knee.

DISCUSSION

DR. E. A. OLIVER: This patient recalls to my mind one whom I saw recently. A woman whom I had treated for erythema nodosum appeared with a second attack. It was similar to the first attack except that several of the older lesions had taken on a warty, condylomatous appearance. On questioning her carefully about self-medication, which she had previously denied having attempted, I discovered that for the past year she had been taking headache capsules containing bromide. Iodides and bromides often produce such nodose lesions.

DR. FRED R. SCHMIDT: I saw a similar case in a syphilitic woman, aged 45, about two years ago. She had been taking various headache powders, some containing bromine, and had also been taking iodides. There were lesions typical of erythema nodosum on both legs, and when the iodine medication was stopped the eruption cleared promptly. Darier gives considerable attention to erythema nodosum due to bromides and iodides.

DR. MAX S. WIEN: When this patient was first seen, the clinical characteristics of erythema nodosum were so evident that I thought that if she had a recurrence it would be worth while to present her. At that time she had a large lesion on one calf with some tendency to central softening, which, however, resolved without suppurating. The fact that when taking iodide she again showed similar lesions I think proves the diagnosis.

KAPOSI'S HEMORRHAGIC SARCOMA. Presented by DR. J. H. MITCHELL.

This patient was presented at the meeting of the Dermatological Conference of the Mississippi Valley, Jan. 20, 1934 and the history is published in the report of that meeting (ARCH. DERMAT. & SYPH. **30**:278 [Aug.] 1934).

She is presented at this time to show the progress of the case. The original lesions have practically disappeared. New lesions, however, have continued to form and are now to be seen on the margin of each palm at the bone of the little finger.

DISCUSSION

DR. A. W. STILLIANS: Did any of the lesions disappear spontaneously?

DR. J. H. MITCHELL: None have disappeared spontaneously so far as I know. New lesions have continued to develop, and most of those given radiotherapy have involuted.

MYXEDEMA (LOCALIZED). Presented by DR. M. H. EBERT and DR. M. J. WOLFF.

Mrs. M. C., a white woman aged 45, was admitted to the Cook County Hospital with a diagnosis of thyrotoxicosis. She was seen in consultation about one month ago because of an infiltration of the skin on the anterior aspects of both legs. No history of its duration could be obtained. The basal metabolic rate on admission was + 60.

Examination revealed an infiltration of the cutis of the lower third of each leg, which was well defined, being raised distally and sloping into normal skin proximally. Permission to perform a biopsy was refused.

Thyroidectomy was performed sixteen days ago.

DISCUSSION

DR. S. W. BECKER: I have seen several such cases, and it is peculiar that various factors in hyperthyroidism and hypothyroidism do not necessarily run parallel. I have seen similar localized myxedema in patients with high basal metabolic rates. The control exerted by the thyroid is a complicated mechanism which is not completely understood.

DR. RUBEN NOMLAND: I think that this case is unusual, for in most of Dr. O'Leary's cases the condition developed following thyroidectomy, and in this instance it preceded thyroidectomy by a year or more.

DR. M. H. EBERT: This case is interesting because clinically the condition is classic localized myxedema and because it occurred in a patient with definite hyperthyroidism (basal metabolic rate, + 60). Many of the patients with symptoms of hyperthyroidism have been operated on, and following that symptoms of myxedema appear, but in this case there was no operative procedure until recently. Another interesting feature about Dr. O'Leary's series and other series is that localized myxedema usually does not appear unless there has been marked disturbance of heart function. Fibrillation has frequently been present and was present in this case. A biopsy should have been made, but the internists in the medical service made too much of taking a specimen and, owing to her great apprehensiveness, the patient refused to permit it.

EPITHELIOMA (BASAL CELL) OF THE EAR OF A NEGRESS. Presented by DR. RUBEN NOMLAND and DR. R. H. SCULL.

This Negress, aged 39, states that her disorder began two years ago following an injury to the left ear. She first noted some swelling and discharge in the external auditory meatus, which were followed by occlusion of the meatus and swelling of the concha. She complains of some pain around the external ear and in the temporal region.

There is now a bluish, indurated swelling involving the left ear, extending into and occluding the external auditory meatus. Within the meatus there is some erosion of the lesion, with exudation of a purosanguineous discharge.

Biopsy on a specimen taken from the edge of the lesion revealed islands of basal cells invading the cutis. The cells stained darker than ordinary basal cells, and in some places there was apparent formation of acini filled with a colloid material. In other areas there was a suggestion of a hyaline matrix, such as is seen in cylindroma. In one place there was a definite indication that the new growth arose from the basal cell layer of the epidermis, but there was also indication that it may have arisen from the adnexa of the skin.

DISCUSSION

DR. S. W. BECKER: I think that the histologic structure is that of a type of tumor concerning which there is a great deal of argument. The cells are of the basal cell type, but I thought that I saw enough encapsulation and other characteristic features to regard the picture as that of the tumor called endothelioma capitis, which has been described as a sweat gland tumor, a sebaceous gland tumor and a tumor originating in the hair follicles. I think that this growth is not the type of basal cell carcinoma that originates from the epidermis.

DR. C. W. FINNERUD: Five or six years ago I showed before the Chicago Dermatological Society a Negro, aged about 70, who had a lesion on the nose of similar histologic characteristics. That lesion had been present since childhood and, from what the patient said, might have been present since infancy. We thought that it might be of nevoid origin. The histologic changes were practically identical with the ones in this case. The man was about the color of this patient, dark but probably not a full-blooded Negro. In many of the epithelial nests there were hyalin-like deposits such as were seen in some of the nests in this case. I think that the tumors in these cases belong with benign basal cell growths, but in the serial sections in my case I was not able to determine the origin definitely. Such growths probably develop from misplaced embryonic cell rests. It is impossible for me accurately to classify these tumors with the basal cell epitheliomas, cylindromas or endotheliomas, but I do not feel that they are of sweat gland origin. Many of the southern physicians will affirm that epitheliomas, at least those of basal cell type, do not occur in full-blooded Negroes.

DR. M. R. CARO: The unusual thing about the tumor is that within some of these nests of cells that resemble basal cells a lumen is present, either in the center or at one side. The material within the lumen resembles red blood corpuscles, but it probably represents fatty degeneration. It will be interesting to stain the material for fat to determine whether or not these lumens are ducts from fat-producing glands, from which the tumor may have originated.

Regarding Dr. Becker's remark that this is not an ordinary basal cell epithelioma derived from the basal layer, fairly conclusive evidence was presented in a recent article (Haythorn, S. R.: Studies on the Histogenesis of the So-Called Basal Cell Carcinoma, *Am. J. Cancer* (Supp.) **15**:1969 [July] 1931) that most basal cell cancers originate from the hair follicles and that connection with the epidermis is usually secondary.

DR. RUBEN NOMLAND: The primary consideration should be from the clinical point of view, and it is difficult for me to conceive of such a firm, infiltrated lesion as this with a history of active growth being anything clinically except a malignant or inflammatory lesion. I think that the results of biopsy effectively rule out the possibility of inflammation, and it remains only to classify the type of malignant growth. The question of cylindroma was considered previously, but in view of the clinical findings I think that that diagnosis is almost out of consideration, although some places in the nests of cells were suggestive. In some areas in the section the tumor cells could be seen to arise from the basal cells, but there was also a suggestion that they might originate from the coil glands. I think that the growth is a basal cell epithelioma arising from the basal cells of the epidermis or the coil glands.

CHRONIC SUPERFICIAL ULCERATION OF THE SCALP. Presented by DR. MAX S. WIEN and DR. MINNIE O. PERLSTEIN.

This Negress, aged 29, was admitted to the Cook County Hospital on Feb. 23, 1934, with a lesion on the scalp of two years' duration, a lesion on the nose of three weeks' duration and a lesion on the dorsum of the right hand of one week's duration.

The involvement of the scalp began with severe pruritus, which was followed by the appearance of vesicles which ruptured and left a raw denuded surface, which was painful and bled easily. There was gradual progression of the condi-

tion without healing. She had acute rhinitis, with the development of blisters about the right nasal orifice. Vesicles also appeared on the back of the right hand, which broke, leaving a small ulcer.

Examination when she was first seen revealed almost complete denudation of the scalp, leaving a red, moist, bleeding surface. At the present time there are large areas of new epithelium over the vertex, also a crusted herpes simplex lesion on the right side of the nose and a healing pyodermic ulcer of the right hand. There is no history of gastro-intestinal disturbance, except for constipation. The patient has marked secondary anemia. The Wassermann reaction of the blood was negative. Examination revealed no involvement of the nasal sinuses.

DISCUSSION

DR. H. M. HEDGE: How deep does the ulceration extend?

DR. MAX S. WIEN: No growth of hair or follicular structure is evident grossly in the areas of ulceration. We have seen this type of ulceration in other cases in the hospital, and one is impressed by the association of it with a lowered constitutional condition. While we get some results from local therapy, we get better results by combining tonic therapy with it.

THROMBOSIS (BILATERAL) OF THE SUPERIOR LABIAL ARTERIES, WITH GANGRENE IN A DIABETIC PATIENT. Reported by DR. CLEVELAND J. WHITE.

A woman, aged 65, had a small furuncle in the upper lip just under the nose. She had had diabetes for several years and followed dietary instructions indifferently. Two days after she picked at this small furuncle bilateral, extensive, progressive thrombosis of the two regional arteries occurred, followed rapidly by gangrene.

The patient was seen by Dr. J. L. Nortell, who recognized at once the unusual clinical picture. Death occurred within eighteen hours after the extension of the process. Dr. Elliott P. Joslin, Professor of Medicine, at Harvard University, stated that he had never observed such a case. McKittrick and Root did not mention such a complication in their textbook on diabetic surgery, and Dr. Root stated that he had never seen such a case in fifteen hundred cases of diabetes with surgical complications.

Necropsy by Dr. Piette confirmed the clinical diagnosis.

PHILADELPHIA PEDIATRIC SOCIETY AND PHILADELPHIA DERMATOLOGICAL SOCIETY

ROBERT L. GILMAN, M.D., *Secretary*

Joint Meeting, Feb. 23, 1934

JACQUES P. GUEQUIERRE, M.D., *Chairman*

TRANSFUSION SYPHILIS. Presented by DR. V. C. GARNER.

This white boy, aged 10 years, was brought to the University Hospital dispensary on Jan. 19, 1934, because of moth-eaten alopecia of several weeks' duration and a patchy depigmentation of the neck (leukoderma colli). There was a history of an emergency transfusion in June 1933 for possible poliomyelitis or transverse myelitis. The donor was a brother, aged 22, who had had no Wassermann test prior to transfusion. Later examination of the donor revealed a history of penile lesions in 1932 with local treatment only. When examined at the University Hospital on January 22, he gave a strongly positive Wassermann reaction. The patient gave strongly positive reactions to the Wassermann, Kahn and Kline precipitation tests.

DISCUSSION

DR. J. H. STOKES: The use of a relative as a donor absolutely does not insure against transmission. It is possible in eighteen minutes to conduct a presumptive Kline test; it is certainly possible within thirty minutes to determine the donor's fitness. It is unpardonable to transmit the disease in this fashion.

DR. R. M. TYSON: What about taking blood from a parent?

DR. J. H. STOKES: At times children escape prenatal infection from their mothers. The father can acquire syphilis between the birth of the child and the time of transfusion; the same thing can apply to the mother. The question as to whether a child who undoubtedly contracted syphilis prenatally can be given a transfusion from a parent is a little harder to answer. It is undesirable to subject any one to the risk of possible superinfection, and certainly a parent as such is not to be regarded as immune from syphilis.

GRANULOMA ANNULARE. Presented by DR. C. S. WRIGHT.

This white boy, aged 7 years, was admitted to the skin clinic of the University Hospital on July 29, 1933, presenting two mildly inflammatory annular lesions on the hands. These were typical lesions of granuloma annulare, having the elevated waxy borders and central depression. One lesion involuted following intravenous injections of a gold compound and roentgen therapy.

DISCUSSION

DR. V. C. GARNER: There is an illuminating article on granuloma annulare by Michael in the February issue of the ARCHIVES OF DERMATOLOGY AND SYHILOLOGY (**29**:189, 1934), dealing with the entire literature. It has been a moot point whether or not the disease is tuberculous in origin. Michael summarizes the literature by stating that probably some cases are tuberculous although the majority are possibly of unknown infectious origin. Only one investigator has been able to isolate the tubercle bacillus, and his findings are not conclusive. From the pediatric standpoint I feel that any patient with granuloma annulare should be thoroughly and exhaustively studied for underlying tuberculosis.

DR. R. FRIEDMAN: Granuloma annulare is usually classified among the tuberculids. Because of that my associates and I had this child examined in the pediatric department, which reported negative findings for tuberculosis clinically. We referred him to the immunologic department for a Mantoux test, and that was reported negative. We had a biopsy done, and the report on the basis of some epithelioid cells was "granuloma annulare." Granuloma annulare is considered among the tuberculids because in some of the cases there is a definite history of tuberculosis and the histologic picture resembles that of tuberculosis. In this case the clinical and laboratory tests were all negative. One of the interesting features is that after we removed by biopsy one of the lesions of granuloma annulare on the dorsum of one hand and took with it a margin of healthy skin, the wound healed and in the scar that subsequently developed there appeared a new lesion of granuloma annulare.

DR. E. P. BACON: If the condition is due to tuberculosis, does one treat the patient for both tuberculosis and granuloma annulare?

DR. J. P. GUEQUIERRE: Numerous conditions have responded to treatment with gold compounds, but as far as I know it has not been effective in pulmonary tuberculosis, although recently a favorable report has come out.

DR. S. S. GREENBAUM: I recently saw a baby with lesions of this sort on the face. Like so many skin lesions, those of granuloma annulare occasionally disappear spontaneously. In my case the lesions disappeared following the daily application of collodion. Of course that does not happen in all cases of granuloma annulare, but occasionally lesions do disappear under what appears to be the mildest sort of application.

DR. J. P. GUEQUIERRE: Several months ago I saw a man of 55 with granuloma annulare. I removed a specimen for biopsy with the cutting current, and by the time the wound had healed the entire lesion had cleared up. He had no treatment.

DR. J. M. SCHILDKRAUT: Some time ago I observed two cases, in a brother and sister, which made me think of the possibility of something contagious. In one of the children poliomyelitis developed, and the lesions cleared up during the attack. When last seen the other child still had granuloma annulare.

JUVENILE PARESIS. Presented by DR. HERMAN BEERMAN.

This white girl, aged 8 years, was undernourished and anemic when admitted to the skin clinic of the University Hospital. The scalp was normal. The frontal bosses were prominent. The pupils reacted poorly to light, and the right was larger than the left. The reflexes were hyperactive. The bones were normal. The upper central incisors were somewhat wedge-shaped. The visual fields were somewhat contracted. Examination of the spinal fluid on Oct. 5, 1933, showed the Wassermann reaction to be 3 plus, and the colloidal gold curve, 4445430000. The Wassermann reaction of the blood was strongly positive. The patient was always rather sickly, but in spite of frequent medical consultation no serologic studies were made. The history further revealed that the mother's blood gave positive serologic reactions.

DISCUSSION

DR. HERMAN BEERMAN: Because the child's visual fields were contracted we treated her with bismarsen. We intend, however, to attempt to give tryparsamide after the fields are checked.

DR. S. S. GREENBAUM: The diagnosis in this case is evidently based on laboratory tests. There are no mental disturbances. I have treated several congenital syphilitic patients by means of malaria, and I see no reason why fever therapy, not necessarily malaria, would not be of great use in this case, particularly in view of the probable paresis sine paresi. I also want to call attention to the physical maldevelopment that has been described recently, a shortening of one or more fingers in cases of congenital syphilis. This child presents a slight shortening of one finger, and I have recently observed this in several other congenital syphilitic patients.

DR. J. H. STOKES: I think that there is a definite purpose in showing this child. The prognosis of juvenile paresis has been regarded as extremely poor because no effort has been made to recognize cases before they reach the deteriorative stage. The response of children is better to intelligent routine therapy, and the use of arsphenamine instead of neoarsphenamine might give a striking result in this child. None the less, it is generally true that the treatment by routine methods should not be carried through to the degree that it usually is. The patients should be early given tryparsamide and fever therapy. If treatment is delayed until signs of degeneration have existed for two years, the prognosis is markedly poorer. These children stand fever therapy. They also take tryparsamide satisfactorily. This child's treatment should be intensified as soon as possible. At 8 years of age she may be eligible for fever therapy. It is inexcusable to allow a child with prenatal syphilis to go under treatment without examination of the spinal fluid, or to wait until after degeneration manifestations appear before applying modern methods of treatment.

DR. C. S. WRIGHT: In the congenital syphilis clinic at the Graduate Hospital my associates and I see, on an average, about 50 children a week. I do not think that we find a positive reaction of the spinal fluid more than once every two or three years. Evidently it is not particularly common, occurring in not over from 3 to 5 per cent of the cases.

DR. V. C. GARNER: I observed a girl of 12 years who had had two hundred injections of a bismuth compound. At the completion of the last course of bismuth therapy the child began to have epileptiform seizures as often as twice a day. Under treatment with tryparsamide the epileptiform seizures have completely dis-

appeared. She has had one hundred and fifty intravenous injections of tryparsamide without any reaction, and there has been a reversal of the reaction of her spinal fluid to complete negativity.

Dr. J. H. Stokes: The influence of an abnormal spinal fluid depends on the age of the child. Jeans showed that about 40 per cent of syphilitic children 1 year old and under have abnormal spinal fluid. In children 12 years of age one can hardly expect to find an abnormal fluid in more than 3 or 4 per cent. If one is going to do lumbar punctures on children under 1 year of age one should get a high percentage of positive reactions.

Dr. D. M. Pillsbury: As I recall the percentage at the Children's Hospital, there were 3 positive reactions in 118 cases. Jeans has pointed out that the Wassermann reaction of the blood is a better indication of the possibility of neurosyphilis in children than in adults. Of course it is entirely possible to have a negative Wassermann reaction of the blood and a positive reaction of the spinal fluid in a child, but not as probable as in an adult.

Dr. S. S. Greenbaum: Several years ago I treated a boy of 13, with tabes, who because he was so markedly ataxic had to be carried in. After he had had a definite number of malaria chills and had been in the hospital for a month or more, he walked out of the hospital practically unaided. The ataxia had practically disappeared. However, in my experience it is unusual to get a result with malaria in adult tabetic patients similar to that obtained in children.

Nevus (?) of the Left Shoulder. Presented by Dr. C. S. Wright and Dr. J. R. Moore.

This patient is presented for opinions as to diagnosis and therapy.

DISCUSSION

Dr. C. G. Jordan (by invitation): I cannot offer any explanation as to the cause except that the condition looks like a contractile scar just like a scar from any burn that has influenced the growth. It is well known that a fracture near the epiphysis in children might stunt the growth of the arm. But I do not know why the nevus is there, or whether it has any influence on the fracture. I suggest orthopedic treatment—excision of the lesion and the same treatment as for any other malformation of bone. The bone will have to be broken in several places, and I think that normal growth will continue. I do not know whether from the x-ray plate one can definitely see that there is no center of ossification at the head of the humerus. I do not think that there is any ankylosis. I have seen the same type of deformity from a scar left by a burn. One does not see such conditions in young children.

Dr. C. S. Wright: This child is a patient of Dr. John R. Moore, the head of the Temple University orthopedic department. He considered for some time doing as Dr. Jordan suggests, namely, performing an operation and trying to separate the soft tissue from the bone and to repair the parts as best he could. However, he hesitated, not knowing just what he was going to run into. He thought perhaps the lesion was a nevus. I frankly admit that it is different from anything I have seen.

Dr. J. H. Stokes: Occasionally one sees associated with morpheiform lesions extraordinary atrophy and shrinkage of the tissue, a wasting away. In some nevi one sees also associated contractures and bony hyperplasia. For instance, in extensive angiomatous processes involving all of one side of the body, one occasionally sees them. However, none of those manifestations look much like this lesion. I incline toward a diagnosis of nevus. The growth of hair certainly suggests something of that sort. I could not feel anything to suggest a morpheiform or sclerodermatous process in the center. I was surprised at the remarkable thickening of the humerus. It looked like osteitis. I wonder if it would not be permissible to take a deep biopsy specimen to see what the histologic examination might bring forth. That would be the proper preliminary step before proceeding to radical orthopedic surgery.

News and Comment

NINTH INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY

The Ninth International Congress of Dermatology and Syphilology will meet in Budapest, Hungary, on Sept. 15 to 21, 1935. Any one desiring to present a paper at the Congress is invited to submit it to Dr. Howard Fox, 140 East Fifty-Fourth Street, New York, the American secretary of the Congress, on or before Jan. 1, 1935. The program of American participation in the Congress has been prepared by a joint committee appointed by the American Dermatological Association and the Section on Dermatology and Syphilology of the American Medical Association, consisting of Oliver Ormsby (chairman), Harold N. Cole, Howard Fox, W. H. Guy, C. Guy Lane, George M. MacKee, Paul O'Leary, John H. Stokes, Fred D. Weidman and Udo J. Wile.

Books Received

TRABAJOS DEL SANATORIO NACIONAL DE FONTILLES. Clinical and Statistical Report of the National Leprosy Sanatorium, Fontilles, Spain, 1932-1933. Dr. P. Montañés, director. Pp. 336.

Book Reviews

Lehrbuch und Atlas der Haut- und Geschlechtskrankheiten, für praktische Arzte und Studierende. By Karl Wilhelm Felix Zieler and Edward Jacobi. Third German edition. Pp., volume 1, 664; volume 2, 181. Price, 48 marks; bound, 65 marks. Berlin: Urban & Schwarzenberg, 1934.

The atlas of Jacobi has long been recognized as one of the most useful collections of illustrations of diseases of the skin. It first appeared about thirty years ago (in 1906) in an English edition under the editorship of the able and beloved J. J. Pringle of London. This volume is the third German edition, edited by Prof. Karl Zieler of Wurzburg. A work on dermatology that has had so long a life and that is still in demand needs hardly any comment. Nevertheless, it is pleasant to revert to Jacobi's atlas and to have the opportunity of recalling its virtues. The present edition is in two volumes, both of which have truly, in the words of the title page, been enlarged and improved. The first volume is a concise but comprehensive and accurate textbook of dermatology. It covers well the whole subject of dermatology and syphilis.

But the chief concern is with the atlas, the second volume. This is, the reviewer believes, taken as a whole, the best atlas of diseases of the skin that is available either to specialists in diseases of the skin or to others. It includes the rarer diseases, but its chief value lies in its lifelike portrayal of cutaneous diseases of all sorts. In excellence, accuracy, technical beauty and the selection of cases to be portrayed, the illustrations leave nothing to be desired. The only difference between looking at these pictures and looking at the actual cases is that one sees usually only the part of the body that is affected and not the whole person, and they are, of course, somewhat reduced in size. But against that it can be said that the illustrations are always available for study, while patients with the diseases are not. The illustrations give as nearly perfect a reproduction of the appearance of actual diseases as it is possible to make. One of the features of the work which deserves emphasis is the price (bound, 65 marks, or about $16). To reproduce in the United States the 342 colored illustrations in the atlas alone would cost more than $34,000 ($100 each). Probably the atlas alone would cost $50,000. This means that at present the publication of such an atlas is out of the question in this country. Fortunately, Jacobi's work makes it unnecessary. The reviewer calls attention more readily to the reasonableness in the price of Jacobi's atlas because of the excessively high prices that prevent the circulation of so many excellent works.

Directory of Dermatologic Societies *

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

W. R. Jaffrey, President, 64 Hughson St., S., Hamilton, Ont.
Basil Bowman, Secretary-Treasurer, 408 Medical Arts Bldg., Hamilton, Ont.
Place: Montreal, Quebec. Time: May 4, 1935.

Royal Society of Medicine, Section of Dermatology

Henry MacCormac, President, 23, Wimpole St., W. 1, London.
W. N. Goldsmith, Secretary, 6, Upper Wimpole St., W. 1, London.

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

Jeffrey C. Michael, Chairman, 1215 Walker Ave., Houston, Texas.
Harry R. Foerster, Secretary, 208 E. Wisconsin Ave., Milwaukee.
Place: Atlantic City. Time: June 10-14, 1935.

American Dermatological Association

Charles M. Williams, President, 114 E. 54th St., New York.
W. H. Guy, Secretary, 500 Penn Ave., Pittsburgh.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Harry F. Anderson, President, 1610, 20th St. N.W., Washington, D. C.
Joseph V. Kennedy, Secretary, 1835 Eye St., Washington, D. C.

Central States Dermatological Association

Joseph Brumberg, President, 528 Delaware Ave., Buffalo.
William F. Hoover, Secretary, 333 Linwood Ave., Buffalo.
Place: Buffalo. Time: 1934.

Iowa and Western Illinois Dermatological Association

J. C. Kessler, President, University Hospital, Iowa City.
Robert E. Jameson, Secretary, 1014 First National Bank Bldg., Davenport, Iowa.

New England Dermatological Society

Rudolph Jacoby, President, 270 Commonwealth Ave., Boston.
J. Harper Blaisdell, Secretary, 5 Bay State Road, Boston.

Southern Medical Association, Section on Dermatology and Syphilology

Thomas W. Murrell, Chairman, 17 E. Grace St., Richmond, Va.
C. C. Dennie, Secretary, Professional Bldg., Kansas City, Mo.
Place: San Antonio, Texas. Time: November, 1934.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

STATE DERMATOLOGIC SOCIETIES

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Ernest K. Stratton, Chairman, 490 Post St., San Francisco.
John M. Graves, Secretary, 909 Hyde St., San Francisco.

Florida Society of Dermatology and Syphilology

Chairman for each meeting is elected from city in which meeting is held.
Elmo D. French, Secretary, 602 Huntington Bldg., Miami.

Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, Maison Blanche Bldg., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

George M. Fisher, Chairman, 264 Genesee St., Utica.
Frank Combes, Secretary, 80 W. 40th St., New York.

Medical Society of the State of Pennsylvania Section on Dermatology

Herbert J. Smith, President, 3303 N. 17th St., Philadelphia.
Robert L. Gilman, Secretary, 1930 Chestnut St., Philadelphia.

Michigan State Medical Society, Section on Dermatology and Syphilology

Robert C. Jamieson, Chairman, 1551 Woodward Ave., Detroit.
A. R. Woodburne, Secretary, Grand Rapids Clinic, Grand Rapids.
Place: Battle Creek. Time: September, 1934.

Minnesota Dermatological Society

D. D. Turnacliff, President, 407 Medical Arts Bldg., Minneapolis.
L. H. Winer, Secretary, 522 Medical Arts Bldg., Minneapolis.
Time: First Wednesday in October, December, February and April.

Oklahoma Dermatological Association

W. A. Showman, President, 108 W. 6th St., Tulsa.
C. L. Brundage, Secretary, 505 Osler Bldg., Oklahoma City.

Texas Dermatological Society

C. F. Lehmann, President, 303 E. Houston St., San Antonio.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.

LOCAL DERMATOLOGIC SOCIETIES

Atlanta Dermatological Society

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

Bronx Dermatological Society

Louis Chargin, Chairman, 1 W. 85th St., New York.
Henry Silver, Secretary, 290 West End Ave., New York.

Brooklyn Dermatological Society

Arthur Persky, President, 1750 Ocean Parkway, Brooklyn.
George F. Price, Secretary, 884 Lincoln Place, Brooklyn.
Time: Third Monday of each month except June, July, August and September.

Buffalo-Rochester Dermatological Society

Earl D. Osborne, President, 471 Delaware Ave., Buffalo.
Richard L. Saunders, Secretary, 33 Linwood Ave., Buffalo.

Chicago Dermatological Society

James H. Mitchell, President, 25 E. Washington St., Chicago.
Max S. Wien, Secretary, 104 S. Michigan Ave., Chicago.

Cincinnati Dermatological Society

Harry L. Claassen, President, Provident Bank Bldg., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

Cleveland Dermatological Society

R. E. Barney, President, 1021 Prospect Ave., Cleveland.
E. W. Netherton, Secretary, 2020 E. 93d St., Cleveland.

Detroit Dermatological Society

H. L. Keim, President, 10 Witherell St., Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

Los Angeles Dermatological Society

Moses Scholtz, Chairman, 1930 Wilshire Blvd., Los Angeles.
Nelson P. Anderson, Secretary, 2007 Wilshire Blvd., Los Angeles.

Manhattan Dermatologic Society

Louis B. Mount, Chairman, 256 State St., Albany, N. Y.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

Alberic Marin, President, 1414 Drummond St., Montreal, Canada.
Paul Poirier, Secretary, 2073 St. Denis St., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

Ray H. Rulison, Chairman, 145 E. 54th St., New York.
E. William Abramowitz, Secretary, 853, 7th Ave., New York.

New York Dermatological Society

Fred Wise, President, 200 W. 59th St., New York.
R. H. Rulison, Secretary, 145 E. 54th St., New York.

Omaha Dermatological Society

J. W. Hellwig, Chairman, 1319 Farnam St., Omaha.
Donald J. Wilson, Secretary, 1216 Medical Arts Bldg., Omaha.

Philadelphia Dermatological Society

Robert L. Gilman, Chairman, 1930 Chestnut St., Philadelphia.
Vaughn C. Garner, Secretary, Greene and Coulter Sts., Philadelphia.

Pittsburgh Dermatological Society

Bernhard A. Goldmann, President, Jenkins's Arcade, Pittsburgh.
J. Cavanaugh, Secretary, 28 Market St., Youngstown, Ohio.

St. Louis Dermatological Society

Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
M. F. Engman, Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

San Francisco Dermatological Society

H. J. Templeton, President, 3115 Webster St., Oakland, Calif.
John M. Graves, Secretary, 909 Hyde St., San Francisco.

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